

which is involved in regulation of transcription at NFE2 sites. Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAFK. The function of MAFK has been established by previous studies. The developmentally regulated expression of the globin genes depends on upstream regulatory elements termed locus control regions (LCRs). LCRs are associated with powerful enhancer activity that is mediated by the transcription factor NFE2 (nuclear factor erythroid-2). NFE2 recognition sites are also present in the gene promoters of 2 heme biosynthetic enzymes, porphobilinogen deaminase (PBGD; 176000) and ferrochelatase (FECH; 177000). NFE2 DNA-binding activity consists of a heterodimer containing an 18-kD Maf protein (MafF, MafG (OMIM Ref. No. 602020), or MafK) and p45 (OMIM Ref. No. 601490). Both subunits are members of the activator protein-1 superfamily of basic leucine zipper (bZip) proteins (see OMIM Ref. No. 165160). Maf homodimers suppress transcription at NFE2 sites. Toki et al. (1997) isolated a cDNA encoding human MAFK. The MAFK gene encodes a 156-amino acid polypeptide which is widely expressed, with highest levels seen in heart, placenta, skeletal muscle, and kidney. Toki



et al. (1997) showed that MAFK could heterodimerize not only with p45, but also with NFE2-related factor 1 (NRF1; 163260) and NFE2-related factor 2 (OMIM Ref. No. 600492); these heterodimers bound to NFE2 sites in vitro. In vivo, MAFK/p45 and MAFK/NRF1 heterodimers stimulated transcription from NFE2 sites. Similar results were found with MAFG. Iwata et al. (1998) showed that MAFK is encoded by 3 exons spanning approximately 10 kb. By use of 2 DNA mapping panels isolated from mice of a recombinant inbred strain set, Peters and Eicher (1994) demonstrated that the ubiquitous subunit is located on mouse chromosome 5. Since this region of the mouse genome shares linkage homology with human chromosome 7q, Peters and Eicher (1994) suggested that human NFE2U is probably located on 7q. Iwata et al. (1998) used FISH to map the MAFK gene to human chromosome 7p22. Motohashi et al. (2000) found that mouse embryos expressing abundant transgene-derived Mafk died of severe anemia, while lines expressing lower levels of small Maf lived to adulthood. Megakaryocytes from the latter overexpressing lines exhibited reduced proplatelet formation and MARE (Maf recognition element)-dependent transcription, phenocopying Mafg null mice (see OMIM Ref. No. Shavit et al.

(1998)). When the Mafg null mice were bred to small Maf-overexpressing transgenic animals, both loss- and gain-of-function phenotypes were reversed

[51974] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51975] Toki, T.; Itoh, J.; Kitazawa, J.; Arai, K.; Hatakeyama, K.; Akasaka, J.; Igarashi, K.; Nomura, N.; Yokoyama, M.; Yamamoto, M.; Ito, E. : Human small Maf proteins form heterodimers with CNC family transcription factors and recognize the NF-E2 motif. *Oncogene* 14: 1901-1910, 1997. ; and

[51976] Motohashi, H.; Katsuoka, F.; Shavit, J. A.; Engel, J. D.; Yamamoto, M. : Positive or negative MARE-dependent transcriptional regulation is determined by the abundance of small Maf proteins.

[51977] Further studies establishing the function and utilities of MAFK are found in John Hopkins OMIM database record ID 600197, and in cited publications numbered 10206-10210 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PBX/knotted 1 Homeobox 1 (PKNOX1, Accession NM\_004571) is another VGAM1505 host target gene.

PKNOX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKNOX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKNOX1 BINDING SITE, designated SEQ ID:10914, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51978] Another function of VGAM1505 is therefore inhibition of PBX/knotted 1 Homeobox 1 (PKNOX1, Accession NM\_004571), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKNOX1. The function of PKNOX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM276.RAP1, GTPase Activating Protein 1 (RAP1GA1, Accession NM\_002885) is another VGAM1505 host target gene. RAP1GA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAP1GA1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP1GA1 BINDING SITE, designated SEQ ID:8795, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51979] Another function of VGAM1505 is therefore inhibition of RAP1, GTPase Activating Protein 1 (RAP1GA1, Accession NM\_002885). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAP1GA1. Retinal Degeneration, Slow (retinitis pigmentosa 7) (RDS, Accession NM\_000322) is another VGAM1505 host target gene. RDS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RDS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDS BINDING SITE, designated SEQ ID:5865, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51980] Another function of VGAM1505 is therefore inhibition of Retinal Degeneration, Slow (retinitis pigmentosa 7) (RDS,

Accession NM\_000322), a gene which may function as an adhesion molecule involved in stabilization and compaction of outer segment disks or in the maintenance of the curvature of the rim. Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDS. The function of RDS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM341. Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM\_114281) is another VGAM1505 host target gene. SCN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN1A BINDING SITE, designated SEQ ID:42831, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51981] Another function of VGAM1505 is therefore inhibition of Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM\_114281). Accordingly, utilities of

VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN1A. T-cell Leukemia, Homeobox 1 (TLX1, Accession NM\_005521) is another VGAM1505 host target gene. TLX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TLX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLX1 BINDING SITE, designated SEQ ID:12046, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51982] Another function of VGAM1505 is therefore inhibition of T-cell Leukemia, Homeobox 1 (TLX1, Accession NM\_005521), a gene which controls the spleen development. Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLX1. The function of TLX1 has been established by previous studies. Kagan et al. (1987) fused human leukemic T cells carrying a t(10;14)(q24;q11) translocation with mouse leukemic T cells and examined the hybrids for genetic markers of human chromosomes 10 and 14. Hybrids containing the human 10q+ chromo-

some had the human genes for terminal deoxynucleotidyltransferase (TDT; 187410), which had been mapped to 10q23–q25, and for the constant region of TCRA (OMIM Ref. No. 186880). Hybrids containing the human 14q– chromosome retained the variable components of the TCRA gene. Thus the 14q11 breakpoint split the TCRA locus in a region between the variable and constant genes. These results suggested to Kagan et al. (1987) that the leukemic process resulted from translocation of the C(alpha) locus to a putative cellular protooncogene located proximal to the breakpoint at 10q24, with resulting deregulation of said oncogene, for which they proposed the name TCL3. Since the 10q+ chromosome retained the TDT gene, they concluded that the TDT locus is proximal to the TCL3 gene, confirming the location to band 10q23–q24. Zutter et al. (1990) cloned the t(10;14) breakpoint from CD3–negative T–cell acute lymphoblastic leukemia (T–ALL) cells. They identified a locus distinct from TDT at 10q24; this locus was not active in a variety of normal or other neoplastic T cells, but recognized an abundant 2.9–kb RNA in a t(10;14) T–cell leukemia. The authors speculated that this locus is a candidate for the putative TCL3 protooncogene. Kennedy et al. (1991)

showed that the 10q24 region encodes a homeo box gene closely related to the developmentally regulated homeotic genes of flies and mammals. The coding capacity of this activated gene, designated HOX11, was undisturbed in a T-cell line carrying the translocation t(7;10)(q35;q24). Hatano et al. (1991) identified the HOX11 gene adjacent to the breakpoint on 10q24 in the t(10;14) translocation of T-ALL. Dube et al. (1991) also implicated the HOX11 gene in the translocation t(10;14)(q24;q11) that occurs in T-ALL. The translocation juxtaposes the TCRD gene in chromosome 14q11 with a breakpoint that lies immediately centromeric of the HOX11 gene. The translocation is presumably catalyzed by recombinases normally involved in the generation of immunoglobulin and TCR diversity. Dube et al. (1991) suggested that this was the first example of a human cancer in which deregulated expression of an unaltered homeo box gene is involved in tumorigenesis. Lu et al. (1991) cloned the TCL3 gene and found that its expression was elevated in leukemic cells harboring the t(10;14) translocation. Sequence analysis confirmed that TCL3 is a homeo box-containing gene. Animal model experiments lend further support to the function of TLX1. HOX11 is an orphan homeobox gene since it is located at



a site outside the 4 mammalian HOX clusters. Whereas the orthodox HOX genes encode a combinatorial system of positional specification along the anterior–posterior axis of the embryo, the function of orphan homeobox genes is less well understood. As indicated by the findings in the translocation t(10;14), juxtaposition of HOX11 to the T-cell receptor gene redirects the expression of the normal HOX11 product to thymocytes. Transgenic mice in which HOX11 is redirected to the thymus develop T-cell lymphoblastic lymphoma–leukemia. Roberts et al. (1994) isolated a mouse Hox11 genomic clone and found that the homeodomain shared complete amino acid identity with human HOX11. The homologous mouse gene also mapped to the syntenic region within mouse chromosome 19. To assess the functional role of Hox11 in the mouse, Roberts et al. (1994) generated Hox11–deficient mice through gene targeting. Homozygous deficient mice had no spleen, but otherwise appeared normal. Hox11 is normally expressed in the splanchnic anlage arising from the splanchnic mesoderm. The homozygous deficient embryos had no cellular organization at the site of the splanchnic development, but all other splanchnic derivatives developed normally. Roberts et al. (1994) concluded

that Hox11 controls the genesis of a single organ; their finding provided new insight into the genetic regulation of morphogenesis. Dear et al. (1995) performed similar studies in 'knockout' mice and found that, in homozygous Hox11-null embryos, spleen formation commences normally up to a specific stage of embryogenesis, at which point the spleen anlage undergoes rapid and complete resorption. Dying spleen cells exhibited characteristics of apoptosis. The authors concluded that Hox11 is not required to initiate spleen development but is essential for the survival of splenic precursors during organogenesis.

[51983] It is appreciated that the abovementioned animal model for TLX1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[51984] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [51985] Hatano, M.; Roberts, C. W. M.; Minden, M.; Crist, W. M.; Korsmeyer, S. J. : Deregulation of a homeobox gene, HOX11, by the t(10;14) in T cell leukemia. Science 253: 79–82, 1991. ; and
- [51986] Roberts, C. W. M.; Shutter, J. R.; Korsmeyer, S. J. : Hox11 controls the genesis of the spleen. Nature 368: 747–750, 1994.
- [51987] Further studies establishing the function and utilities of TLX1 are found in John Hopkins OMIM database record ID 186770, and in cited publications numbered 5678–5686 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Centaurin, Gamma 2 (CENTG2, Accession NM\_014914) is another VGAM1505 host target gene. CENTG2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CENTG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTG2 BINDING SITE, designated SEQ ID:17155, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.
- [51988] Another function of VGAM1505 is therefore inhibition of

Centaurin, Gamma 2 (CENTG2, Accession NM\_014914). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTG2. DC-TM4F2 (Accession NM\_030927) is another VGAM1505 host target gene. DC-TM4F2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DC-TM4F2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DC-TM4F2 BINDING SITE, designated SEQ ID:25196, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51989] Another function of VGAM1505 is therefore inhibition of DC-TM4F2 (Accession NM\_030927). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DC-TM4F2. DKFZP566K0524 (Accession XM\_045128) is another VGAM1505 host target gene. DKFZP566K0524 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566K0524, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566K0524 BINDING SITE, designated SEQ ID:34372, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51990] Another function of VGAM1505 is therefore inhibition of DKFZP566K0524 (Accession XM\_045128). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566K0524. KIAA0062 (Accession XM\_046677) is another VGAM1505 host target gene. KIAA0062 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0062, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0062 BINDING SITE, designated SEQ ID:34792, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51991] Another function of VGAM1505 is therefore inhibition of KIAA0062 (Accession XM\_046677). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0062. KIAA0153 (Accession NM\_015140) is another VGAM1505 host target gene. KIAA0153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0153 BINDING SITE, designated SEQ ID:17496, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51992] Another function of VGAM1505 is therefore inhibition of KIAA0153 (Accession NM\_015140). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0153. KIAA0825 (Accession XM\_027906) is another VGAM1505 host target gene. KIAA0825 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0825, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0825 BINDING SITE, designated SEQ ID:30589, to the

nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51993] Another function of VGAM1505 is therefore inhibition of KIAA0825 (Accession XM\_027906). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0825. KIAA1036 (Accession NM\_014909) is another VGAM1505 host target gene. KIAA1036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1036 BINDING SITE, designated SEQ ID:17131, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51994] Another function of VGAM1505 is therefore inhibition of KIAA1036 (Accession NM\_014909). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1036. KIAA1437 (Accession XM\_026998) is another VGAM1505 host target gene. KIAA1437 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1437 BINDING SITE, designated SEQ ID:30382, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51995] Another function of VGAM1505 is therefore inhibition of KIAA1437 (Accession XM\_026998). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1437. KIAA1854 (Accession XM\_049884) is another VGAM1505 host target gene. KIAA1854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35523, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51996] Another function of VGAM1505 is therefore inhibition of KIAA1854 (Accession XM\_049884). Accordingly, utilities



of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. MGC11352 (Accession XM\_035941) is another VGAM1505 host target gene. MGC11352 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC11352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11352 BINDING SITE, designated SEQ ID:32354, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51997] Another function of VGAM1505 is therefore inhibition of MGC11352 (Accession XM\_035941). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11352. MGC26954 (Accession NM\_145025) is another VGAM1505 host target gene. MGC26954 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC26954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC26954 BINDING SITE, designated SEQ ID:29639, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51998] Another function of VGAM1505 is therefore inhibition of MGC26954 (Accession NM\_145025). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC26954. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM\_028840) is another VGAM1505 host target gene. PPP1R16B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R16B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R16B BINDING SITE, designated SEQ ID:30763, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51999] Another function of VGAM1505 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM\_028840). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PPP1R16B. RAB17, Member RAS Oncogene Family (RAB17, Accession NM\_022449) is another VGAM1505 host target gene. RAB17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB17 BINDING SITE, designated SEQ ID:22785, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[52000] Another function of VGAM1505 is therefore inhibition of RAB17, Member RAS Oncogene Family (RAB17, Accession NM\_022449). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB17. Ring Finger Protein 38 (RNF38, Accession NM\_022781) is another VGAM1505 host target gene. RNF38 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF38, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF38 BINDING SITE, des-

ignated SEQ ID:23063, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[52001] Another function of VGAM1505 is therefore inhibition of Ring Finger Protein 38 (RNF38, Accession NM\_022781). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF38. SEC22C (Accession NM\_004206) is another VGAM1505 host target gene. SEC22C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC22C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC22C BINDING SITE, designated SEQ ID:10403, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[52002] Another function of VGAM1505 is therefore inhibition of SEC22C (Accession NM\_004206). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC22C. LOC146520 (Accession XM\_085492) is another

VGAM1505 host target gene. LOC146520 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146520 BINDING SITE, designated SEQ ID:38190, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[52003] Another function of VGAM1505 is therefore inhibition of LOC146520 (Accession XM\_085492). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146520. LOC154930 (Accession XM\_088080) is another VGAM1505 host target gene. LOC154930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154930 BINDING SITE, designated SEQ ID:39503, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[52004] Another function of VGAM1505 is therefore inhibition of LOC154930 (Accession XM\_088080). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154930. LOC197285 (Accession XM\_113752) is another VGAM1505 host target gene. LOC197285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197285 BINDING SITE, designated SEQ ID:42414, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[52005] Another function of VGAM1505 is therefore inhibition of LOC197285 (Accession XM\_113752). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197285. LOC221584 (Accession XM\_168132) is another VGAM1505 host target gene. LOC221584 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221584, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221584 BINDING SITE, designated SEQ ID:45041, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[52006] Another function of VGAM1505 is therefore inhibition of LOC221584 (Accession XM\_168132). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221584. LOC253782 (Accession XM\_171023) is another VGAM1505 host target gene. LOC253782 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253782 BINDING SITE, designated SEQ ID:45796, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[52007] Another function of VGAM1505 is therefore inhibition of LOC253782 (Accession XM\_171023). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC253782. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1506 (VGAM1506) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52008] VGAM1506 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1506 was detected is described hereinabove with reference to Figs. 1–8.

[52009] VGAM1506 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Aphid Lethal Paralysis Virus. VGAM1506 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52010] VGAM1506 gene encodes a VGAM1506 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1506 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1506 precursor RNA is designated SEQ ID:1492, and is provided hereinbelow with ref–



erence to the sequence listing part. Nucleotide sequence SEQ ID:1492 is located at position 8885 relative to the genome of Aphid Lethal Paralysis Virus.

[52011] VGAM1506 precursor RNA folds onto itself, forming VGAM1506 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52012] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1506 folded precursor RNA into VGAM1506 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1506 RNA is designated SEQ ID:4217, and is provided hereinbelow with reference to the sequence listing part.

[52013] VGAM1506 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1506 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1506 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52014] VGAM1506 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1506 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1506 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1506 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1506 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52015] The complementary binding of VGAM1506 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1506 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1506 host target RNA into VGAM1506 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52016] It is appreciated that VGAM1506 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1506 host target genes. The mRNA of each one of this plurality of VGAM1506 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1506 RNA, herein designated VGAM RNA, and which when bound by VGAM1506 RNA causes

inhibition of translation of respective one or more VGAM1506 host target proteins.

[52017] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1506 gene, herein designated VGAM GENE, on one or more VGAM1506 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52018] It is yet further appreciated that a function of VGAM1506 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1506 include diagnosis, prevention and

treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1506 correlate with, and may be deduced from, the identity of the host target genes which VGAM1506 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52019] Nucleotide sequences of the VGAM1506 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1506 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1506 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1506 are further described hereinbelow with reference to Table 1.

[52020] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1506 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1506 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52021] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1506 gene, herein designated VGAM is inhibition of expression of VGAM1506 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1506 correlate with, and may be deduced from, the identity of the target genes which VGAM1506 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52022] Chloride Channel 3 (CLCN3, Accession NM\_001829) is a VGAM1506 host target gene. CLCN3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CLCN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN3 BINDING SITE, designated SEQ ID:7567, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52023] A function of VGAM1506 is therefore inhibition of Chloride Channel 3 (CLCN3, Accession NM\_001829), a gene which play a role in the neural cell function through regulation of membrane excitability. Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCN3. The function of CLCN3 and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM1332.CAMP Responsive Element Binding Protein-like 2 (CREBL2, Accession NM\_001310) is another VGAM1506 host target gene. CREBL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CREBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CREBL2 BINDING SITE, designated SEQ ID:6995, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52024] Another function of VGAM1506 is therefore inhibition of CAMP Responsive Element Binding Protein-like 2 (CREBL2, Accession NM\_001310). Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CREBL2. CRIPT (Accession XM\_057669) is another VGAM1506 host target gene. CRIPT BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CRIPT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of CRIPT BINDING SITE, designated SEQ ID:36539, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52025] Another function of VGAM1506 is therefore inhibition of CRIPT (Accession XM\_057669). Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRIPT. FLJ10989 (Accession NM\_018292) is another VGAM1506 host target gene. FLJ10989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10989 BINDING SITE, designated SEQ ID:20282, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52026] Another function of VGAM1506 is therefore inhibition of FLJ10989 (Accession NM\_018292). Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10989. FLJ22794 (Accession XM\_166220) is another



VGAM1506 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44025, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52027] Another function of VGAM1506 is therefore inhibition of FLJ22794 (Accession XM\_166220). Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. KIAA0445 (Accession NM\_014675) is another VGAM1506 host target gene. KIAA0445 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0445 BINDING SITE, designated SEQ ID:16145, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52028] Another function of VGAM1506 is therefore inhibition of KIAA0445 (Accession NM\_014675). Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0445. MGC12760 (Accession NM\_032723) is another VGAM1506 host target gene. MGC12760 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC12760, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12760 BINDING SITE, designated SEQ ID:26447, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52029] Another function of VGAM1506 is therefore inhibition of MGC12760 (Accession NM\_032723). Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12760. Protein-O-mannosyltransferase 1 (POMT1, Accession NM\_007171) is another VGAM1506 host target gene. POMT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POMT1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POMT1 BINDING SITE, designated SEQ ID:14019, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52030] Another function of VGAM1506 is therefore inhibition of Protein-O-mannosyltransferase 1 (POMT1, Accession NM\_007171). Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POMT1. LOC144266 (Accession XM\_084795) is another VGAM1506 host target gene. LOC144266 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144266 BINDING SITE, designated SEQ ID:37711, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52031] Another function of VGAM1506 is therefore inhibition of LOC144266 (Accession XM\_084795). Accordingly, utilities

of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144266. LOC149579 (Accession XM\_048743) is another VGAM1506 host target gene. LOC149579 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149579, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149579 BINDING SITE, designated SEQ ID:35241, to the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, also designated SEQ ID:4217.

[52032] Another function of VGAM1506 is therefore inhibition of LOC149579 (Accession XM\_048743). Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149579. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1507 (VGAM1507) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52033] VGAM1507 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1507 was detected is described hereinabove with reference to Figs. 1–8.

[52034] VGAM1507 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Aphid Lethal Paralysis Virus. VGAM1507 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52035] VGAM1507 gene encodes a VGAM1507 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1507 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1507 precursor RNA is designated SEQ ID:1493, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1493 is located at position 4389 relative to the genome of Aphid Lethal Paralysis Virus.

[52036] VGAM1507 precursor RNA folds onto itself, forming VGAM1507 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52037] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1507 folded precursor RNA into VGAM1507 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1507 RNA is designated SEQ ID:4218, and is provided hereinbelow with reference to the sequence listing part.

[52038] VGAM1507 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1507 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1507 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[52039] VGAM1507 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1507 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1507 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1507 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1507 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52040] The complementary binding of VGAM1507 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1507 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1507 host target RNA into VGAM1507 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52041] It is appreciated that VGAM1507 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1507 host target genes. The mRNA of each one of this plurality of VGAM1507 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1507 RNA, herein designated VGAM RNA, and which when bound by VGAM1507 RNA causes inhibition of translation of respective one or more VGAM1507 host target proteins.

[52042] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1507 gene, herein designated VGAM GENE, on one or more VGAM1507 host target gene, herein designated



VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52043] It is yet further appreciated that a function of VGAM1507 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1507 include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1507 correlate with, and may be deduced from, the identity of the host target genes which VGAM1507 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52044] Nucleotide sequences of the VGAM1507 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1507 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1507 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1507 are further  
described hereinbelow with reference to Table 1.

[52045] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1507 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1507 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[52046] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1507 gene, herein designated VGAM is  
inhibition of expression of VGAM1507 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1507 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1507  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[52047] C-type (calcium dependent, carbohydrate-recognition do-  
main) Lectin, Superfamily Member 5 (CLECSF5, Accession

NM\_013252) is a VGAM1507 host target gene. CLECSF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLECSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF5 BINDING SITE, designated SEQ ID:14921, to the nucleotide sequence of VGAM1507 RNA, herein designated VGAM RNA, also designated SEQ ID:4218.

[52048] A function of VGAM1507 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252). Accordingly, utilities of VGAM1507 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF5. F-box and Leucine-rich Repeat Protein 5 (FBXL5, Accession NM\_033535) is another VGAM1507 host target gene. FBXL5 BINDING SITE1 and FBXL5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FBXL5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FBXL5 BINDING SITE1 and FBXL5 BINDING SITE2, designated SEQ ID:27302 and SEQ ID:14460 respectively, to the nucleotide sequence of VGAM1507 RNA, herein designated VGAM RNA, also designated SEQ ID:4218.

[52049] Another function of VGAM1507 is therefore inhibition of F-box and Leucine-rich Repeat Protein 5 (FBXL5, Accession NM\_033535), a gene which is a putative SCF ubiquitin ligase subunit involved in protein degradation. Accordingly, utilities of VGAM1507 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXL5. The function of FBXL5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM61. Deiodinase, Iodothyronine, Type II (DIO2, Accession NM\_000793) is another VGAM1507 host target gene. DIO2 BINDING SITE1 and DIO2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DIO2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIO2 BINDING SITE1 and DIO2 BINDING SITE2,

designated SEQ ID:6453 and SEQ ID:15163 respectively, to the nucleotide sequence of VGAM1507 RNA, herein designated VGAM RNA, also designated SEQ ID:4218.

[52050] Another function of VGAM1507 is therefore inhibition of Deiodinase, Iodothyronine, Type II (DIO2, Accession NM\_000793). Accordingly, utilities of VGAM1507 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIO2. RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM\_088733) is another VGAM1507 host target gene. RAB40A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB40A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB40A BINDING SITE, designated SEQ ID:39926, to the nucleotide sequence of VGAM1507 RNA, herein designated VGAM RNA, also designated SEQ ID:4218.

[52051] Another function of VGAM1507 is therefore inhibition of RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM\_088733). Accordingly, utilities of VGAM1507 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB40A. Fig. 1 further

provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1508 (VGAM1508) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52052] VGAM1508 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1508 was detected is described hereinabove with reference to Figs. 1–8.

[52053] VGAM1508 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus V. VGAM1508 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52054] VGAM1508 gene encodes a VGAM1508 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1508 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1508 precursor RNA is designated SEQ ID:1494, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1494 is located at position 7772 relative to the genome of Potato Virus V.

[52055] VGAM1508 precursor RNA folds onto itself, forming VGAM1508 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52056] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1508 folded precursor RNA into VGAM1508 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1508 RNA is designated SEQ ID:4219, and is provided hereinbelow with reference to the sequence listing part.

[52057] VGAM1508 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1508 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1508 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52058] VGAM1508 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1508 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1508 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1508 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1508 host target RNA,



herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[52059] The complementary binding of VGAM1508 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1508 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1508 host target RNA into VGAM1508 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52060] It is appreciated that VGAM1508 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1508 host target genes. The mRNA of each one of this plurality of VGAM1508 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1508 RNA, herein designated VGAM RNA, and which when bound by VGAM1508 RNA causes inhibition of translation of respective one or more

VGAM1508 host target proteins.

[52061] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1508 gene, herein designated VGAM GENE, on one or more VGAM1508 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52062] It is yet further appreciated that a function of VGAM1508 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of viral infection by Potato Virus V. Specific

functions, and accordingly utilities, of VGAM1508 correlate with, and may be deduced from, the identity of the host target genes which VGAM1508 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52063] Nucleotide sequences of the VGAM1508 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1508 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1508 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1508 are further described hereinbelow with reference to Table 1.

[52064] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1508 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1508 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52065] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1508 gene, herein designated VGAM is inhibition of expression of VGAM1508 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1508 correlate with, and may be deduced from, the identity of the target genes which VGAM1508 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52066] Beta-site APP-cleaving Enzyme (BACE, Accession NM\_012104) is a VGAM1508 host target gene. BACE BINDING SITE1 and BACE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BACE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BACE BINDING SITE1 and BACE BINDING SITE2, designated SEQ ID:14419 and SEQ ID:29087 respectively, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52067] A function of VGAM1508 is therefore inhibition of Beta-site APP-cleaving Enzyme (BACE, Accession NM\_012104), a gene which is responsible for the proteolytic processing of the amyloid precursor protein. Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BACE. The function of BACE and its association with various dis-

eases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173.DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM\_006892) is another VGAM1508 host target gene. DNMT3B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DNMT3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT3B BINDING SITE, designated SEQ ID:13762, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52068] Another function of VGAM1508 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM\_006892), a gene which is required for genome wide de novo methylation. Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT3B. The function of DNMT3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM280.Fibromodulin (FMOD, Accession

NM\_002023) is another VGAM1508 host target gene.

FMOD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FMOD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FMOD BINDING SITE, designated SEQ ID:7770, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52069] Another function of VGAM1508 is therefore inhibition of Fibromodulin (FMOD, Accession NM\_002023), a gene which affects the rate of fibrils formation. Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FMOD. The function of FMOD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM39. Growth Arrest-specific 1 (GAS1, Accession NM\_002048) is another VGAM1508 host target gene. GAS1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GAS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of GAS1 BINDING SITE, designated SEQ ID:7799, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52070] Another function of VGAM1508 is therefore inhibition of Growth Arrest-specific 1 (GAS1, Accession NM\_002048), a gene which blocks entry to S phase and prevents cycling of normal and transformed cells and thereby is a putative tumor suppressor gene.. Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAS1. The function of GAS1 has been established by previous studies. Growth arrest-specific genes were cloned from mRNAs unique to quiescent, serum-starved NIH 3T3 mouse fibroblasts (Schneider et al., 1988). Webb et al. (1992) mapped the Gas-1 gene to mouse chromosome 13 by in situ hybridization. Colombo et al. (1992) showed linkage of Gas-1 to markers on mouse chromosome 13 in a region that contains 8 loci that are conserved in human 5q, mainly 5q11-q14. Gas-1 is close to the IL9 gene (OMIM Ref. No. 146931), for example. On this basis, Webb et al. (1992) predicted that the GAS1 gene in man is located on 5q. However, the prediction proved not to be

true. Evdokiou et al. (1993) localized the human GAS1 gene to 9q21.3–q22 by tritium–labeled in situ hybridization. DNA from human–rodent somatic cell hybrids was used to verify the location of GAS1 to human chromosome 9. They stated that GAS1 was the first gene to be mapped to both human chromosome 9 and mouse chromosome 13. The location of GAS1 at a site of deletion in myeloid malignancies, together with the demonstration that GAS1 suppresses DNA synthesis, suggested that it is a tumor suppressor gene. Del Sal et al. (1994) demonstrated that overexpression of the human GAS1 gene is able to block cell proliferation in lung and bladder carcinoma cell lines, but not in an osteosarcoma cell line or in an adenovirus–type–5 transformed cell line. Del Sal et al. (1992) had previously shown that simian virus 40–transformed NIH 3T3 cells are also refractory to murine GAS1 overexpression, suggesting that the retinoblastoma and/or p53 gene products have an active role in mediating the growth–suppressing effect of GAS1. By in situ hybridization, Del Sal et al. (1994) mapped the GAS1 gene to 9q21.3–q22.1 in a region considered to be a fragile site. Observations suggesting involvement of this area in bladder carcinoma were cited.



[52071] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52072] Del Sal, G.; Ruaro, M. E.; Philipson, L.; Schneider, C. : The growth arrest-specific gene, *gas1*, is involved in growth suppression. *Cell* 70: 595–607, 1992. ; and

[52073] Schneider, C.; King, R. M.; Philipson, L. : Genes specifically expressed at growth arrest of mammalian cells. *Cell* 54: 787–793, 1988.

[52074] Further studies establishing the function and utilities of GAS1 are found in John Hopkins OMIM database record ID 139185, and in cited publications numbered 2188–2193 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Guanine Nucleotide Binding Protein (G protein), Alpha Z Polypeptide (GNAZ, Accession NM\_002073) is another VGAM1508 host target gene. GNAZ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAZ BINDING SITE, designated SEQ ID:7846, to the nucleotide sequence of VGAM1508 RNA, herein

designated VGAM RNA, also designated SEQ ID:4219.

[52075] Another function of VGAM1508 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Z Polypeptide (GNAZ, Accession NM\_002073), a gene which functions as modulator or transducer in various trans-membrane signaling systems. Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAZ. The function of GNAZ has been established by previous studies. By cDNA cloning, Blatt et al. (1988) identified a G protein-encoding gene which they called G(z-alpha) and symbolized GNAZ. The corresponding protein was found to differ strikingly from other G-alpha subunits in amino acid sequence in a number of regions, and it appeared to be highly enriched in neural tissue (Fong et al., 1988; Matsuoka et al., 1988). Blatt et al. (1988) assigned the GNAZ locus to chromosome 22 by hybridization to the DNA from a panel of rodent-human cell hybrids. By in situ hybridization, Wilkie et al. (1992) demonstrated that the GNAZ gene is located in band 22q11. By the analysis of RFLVs in an interspecific backcross, they showed that the corresponding gene is located on mouse chromosome 10. Budarf et al. (1991) further narrowed the localization to

22q11.2 by fluorescence in situ hybridization on reverse banded metaphase chromosomes. They confirmed the localization by means of a regional mapping panel of somatic cell hybrids.

[52076] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52077] Blatt, C.; Eversole-Cire, P.; Cohn, V. H.; Zollman, S.; Fournier, R. E. K.; Mohandas, L. T.; Nesbitt, M.; Lugo, T.; Jones, D. T.; Reed, R. R.; Weiner, L. P.; Sparkes, R. S.; Simon, M. I. : Chromosomal localization of genes encoding guanine nucleotide-binding protein subunits in mouse and human. Proc. Nat. Acad. Sci. 85: 7642-7646, 1988. ; and

[52078] Wilkie, T. M.; Gilbert, D. J.; Olsen, A. S.; Chen, X.-N.; Amatruda, T. T.; Korenberg, J. R.; Trask, B. J.; de Jong, P.; Reed, R. R.; Simon, M. I.; Jenkins, N. A.; Copeland, N. G. : Evolu.

[52079] Further studies establishing the function and utilities of GNAZ are found in John Hopkins OMIM database record ID 139160, and in cited publications numbered 474 and 2184-2186 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence. Acetyl-Coenzyme A Acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (ACAA2, Accession XM\_166287) is another VGAM1508 host target gene.

ACAA2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ACAA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACAA2 BINDING SITE, designated SEQ ID:44095, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52080] Another function of VGAM1508 is therefore inhibition of Acetyl-Coenzyme A Acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (ACAA2, Accession XM\_166287). Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACAA2. Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM\_031409) is another VGAM1508 host target gene. CCR6 BINDING SITE1 and CCR6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCR6, corresponding to HOST TARGET binding sites such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR6 BINDING SITE1 and CCR6 BINDING SITE2, designated SEQ ID:25369 and SEQ ID:10576 respectively, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52081] Another function of VGAM1508 is therefore inhibition of Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM\_031409). Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR6. FLJ20034 (Accession NM\_017630) is another VGAM1508 host target gene. FLJ20034 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20034 BINDING SITE, designated SEQ ID:19133, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52082] Another function of VGAM1508 is therefore inhibition of FLJ20034 (Accession NM\_017630). Accordingly, utilities of

VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20034. Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010) is another VGAM1508 host target gene. MAP2K4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP2K4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K4 BINDING SITE, designated SEQ ID:8915, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52083] Another function of VGAM1508 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010). Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K4. MGC35558 (Accession NM\_145013) is another VGAM1508 host target gene. MGC35558 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC35558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC35558 BINDING SITE, designated SEQ ID:29616, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52084] Another function of VGAM1508 is therefore inhibition of MGC35558 (Accession NM\_145013). Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC35558. Serum/glucocorticoid Regulated Kinase-like (SGKL, Accession NM\_013257) is another VGAM1508 host target gene. SGKL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SGKL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SGKL BINDING SITE, designated SEQ ID:14926, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52085] Another function of VGAM1508 is therefore inhibition of Serum/glucocorticoid Regulated Kinase-like (SGKL, Accession NM\_013257). Accordingly, utilities of VGAM1508 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with SGKL. Synaptotagmin XIII (SYT13, Accession XM\_167880) is another VGAM1508 host target gene. SYT13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SYT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYT13 BINDING SITE, designated SEQ ID:44890, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52086] Another function of VGAM1508 is therefore inhibition of Synaptotagmin XIII (SYT13, Accession XM\_167880). Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYT13. LOC197358 (Accession XM\_113872) is another VGAM1508 host target gene. LOC197358 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC197358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-



cleotide sequences of LOC197358 BINDING SITE, designated SEQ ID:42512, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52087] Another function of VGAM1508 is therefore inhibition of LOC197358 (Accession XM\_113872). Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197358. LOC256230 (Accession XM\_173371) is another VGAM1508 host target gene. LOC256230 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256230, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256230 BINDING SITE, designated SEQ ID:46540, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52088] Another function of VGAM1508 is therefore inhibition of LOC256230 (Accession XM\_173371). Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256230. LOC256231 (Accession XM\_173372) is an-

other VGAM1508 host target gene. LOC256231 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256231 BINDING SITE, designated SEQ ID:46542, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52089] Another function of VGAM1508 is therefore inhibition of LOC256231 (Accession XM\_173372). Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256231. LOC92539 (Accession XM\_045632) is another VGAM1508 host target gene. LOC92539 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92539, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92539 BINDING SITE, designated SEQ ID:34501, to the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, also designated SEQ ID:4219.

[52090] Another function of VGAM1508 is therefore inhibition of LOC92539 (Accession XM\_045632). Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92539. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1509 (VGAM1509) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52091] VGAM1509 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1509 was detected is described hereinabove with reference to Figs. 1–8.

[52092] VGAM1509 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus V. VGAM1509 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52093] VGAM1509 gene encodes a VGAM1509 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1509 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1509 precursor RNA is designated SEQ ID:1495, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1495 is located at position 8444 relative to the genome of Potato Virus V.

[52094] VGAM1509 precursor RNA folds onto itself, forming VGAM1509 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52095] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1509 folded precursor RNA into VGAM1509 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1509 RNA is designated SEQ ID:4220, and is provided hereinbelow with reference to the sequence listing part.

[52096] VGAM1509 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1509 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1509 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[52097] VGAM1509 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1509 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1509 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1509 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1509 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52098] The complementary binding of VGAM1509 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1509 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1509 host target RNA into VGAM1509 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52099] It is appreciated that VGAM1509 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1509 host target genes. The mRNA of each one of this plurality of VGAM1509 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1509 RNA, herein designated VGAM RNA, and which when bound by VGAM1509 RNA causes inhibition of translation of respective one or more VGAM1509 host target proteins.

[52100] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1509 gene, herein designated VGAM GENE, on one or more VGAM1509 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52101] It is yet further appreciated that a function of VGAM1509 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1509 include diagnosis, prevention and treatment of viral infection by Potato Virus V. Specific functions, and accordingly utilities, of VGAM1509 correlate with, and may be deduced from, the identity of the host target genes which VGAM1509 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52102] Nucleotide sequences of the VGAM1509 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1509 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1509 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1509 are further described hereinbelow with reference to Table 1.

[52103] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1509 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1509 RNA, herein designated VGAM RNA, are described hereinbelow



with reference to Table 2.

[52104] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1509 gene, herein designated VGAM is inhibition of expression of VGAM1509 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1509 correlate with, and may be deduced from, the identity of the target genes which VGAM1509 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52105] Protein Kinase, CAMP-dependent, Catalytic, Beta (PRKACB, Accession NM\_002731) is a VGAM1509 host target gene. PRKACB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKACB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKACB BINDING SITE, designated SEQ ID:8601, to the nucleotide sequence of VGAM1509 RNA, herein designated VGAM RNA, also designated SEQ ID:4220.

[52106] A function of VGAM1509 is therefore inhibition of Protein Kinase, CAMP-dependent, Catalytic, Beta (PRKACB, Accession NM\_002731), a gene which is the catalytic beta sub-

unit of cAMP-dependent protein kinase (PKA). Accordingly, utilities of VGAM1509 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKACB. The function of PRKACB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM795. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1510 (VGAM1510) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52107] VGAM1510 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1510 was detected is described hereinabove with reference to Figs. 1–8.

[52108] VGAM1510 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus V.

VGAM1510 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52109] VGAM1510 gene encodes a VGAM1510 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1510 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1510 precursor RNA is designated SEQ ID:1496, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1496 is located at position 6444 relative to the genome of Potato Virus V.

[52110] VGAM1510 precursor RNA folds onto itself, forming VGAM1510 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52111] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1510 folded precursor RNA into VGAM1510 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1510 RNA is designated SEQ ID:4221, and is provided hereinbelow with reference to the sequence listing part.

[52112] VGAM1510 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1510 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52113] VGAM1510 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1510 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1510 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52114] The complementary binding of VGAM1510 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1510 host target RNA into VGAM1510 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52115] It is appreciated that VGAM1510 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1510 host target genes. The mRNA of each one of this plurality of VGAM1510 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1510 RNA, herein designated VGAM RNA, and which when bound by VGAM1510 RNA causes inhibition of translation of respective one or more VGAM1510 host target proteins.

[52116] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1510 gene, herein designated VGAM GENE, on one or more VGAM1510 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[52117] It is yet further appreciated that a function of VGAM1510 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of viral infection by Potato Virus V. Specific functions, and accordingly utilities, of VGAM1510 correlate with, and may be deduced from, the identity of the host target genes which VGAM1510 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52118] Nucleotide sequences of the VGAM1510 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1510 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1510 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1510 are further described hereinbelow with reference to Table 1.

[52119] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1510 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1510 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52120] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1510 gene, herein designated VGAM is inhibition of expression of VGAM1510 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1510 correlate with, and may be deduced from, the identity of the target genes which VGAM1510 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52121] Calcium Channel, Voltage-dependent, Beta 1 Subunit (CACNB1, Accession NM\_000723) is a VGAM1510 host target gene. CACNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CACNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNB1 BINDING SITE, designated SEQ ID:6387, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52122] A function of VGAM1510 is therefore inhibition of Calcium



Channel, Voltage-dependent, Beta 1 Subunit (CACNB1, Accession NM\_000723), a gene which may not only play an important role in the transport/insertion of the alpha-1S subunit into the membrane. Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNB1. The function of CACNB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM114. inositol(myo)-1(or 4)-monophosphatase 1 (IMPA1, Accession NM\_005536) is another VGAM1510 host target gene. IMPA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IMPA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMPA1 BINDING SITE, designated SEQ ID:12055, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52123] Another function of VGAM1510 is therefore inhibition of inositol(myo)-1(or 4)-monophosphatase 1 (IMPA1, Accession NM\_005536), a gene which is responsible for the

provision of inositol required for synthesis of phosphatidylinositol and polyphosphoinositides. Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMPA1. The function of IMPA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM134. Tuftelin 1 (TUFT1, Accession NM\_020127) is another VGAM1510 host target gene. TUFT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUFT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUFT1 BINDING SITE, designated SEQ ID:21319, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52124] Another function of VGAM1510 is therefore inhibition of Tuftelin 1 (TUFT1, Accession NM\_020127), a gene which appears to play a role in cytokinesis, cell shape, and specialized functions such as secretion and capping. Accordingly, utilities of VGAM1510 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with TUFT1. The function of TUFT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1152.MGC13138

(Accession NM\_033410) is another VGAM1510 host target gene. MGC13138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13138 BINDING SITE, designated SEQ ID:27233, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52125] Another function of VGAM1510 is therefore inhibition of MGC13138 (Accession NM\_033410). Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13138. RAB3A Interacting Protein (rabin3)-like 1 (RAB3IL1, Accession NM\_013401) is another VGAM1510 host target gene. RAB3IL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by RAB3IL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB3IL1 BINDING SITE, designated SEQ ID:15065, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52126] Another function of VGAM1510 is therefore inhibition of RAB3A Interacting Protein (rabin3)-like 1 (RAB3IL1, Accession NM\_013401). Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB3IL1. Ring Finger Protein (C3HC4 type) 8 (RNF8, Accession NM\_003958) is another VGAM1510 host target gene. RNF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF8 BINDING SITE, designated SEQ ID:10099, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52127] Another function of VGAM1510 is therefore inhibition of

Ring Finger Protein (C3HC4 type) 8 (RNF8, Accession NM\_003958). Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF8. Zinc Finger Protein 323 (ZNF323, Accession NM\_030899) is another VGAM1510 host target gene. ZNF323 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF323 BINDING SITE, designated SEQ ID:25170, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52128] Another function of VGAM1510 is therefore inhibition of Zinc Finger Protein 323 (ZNF323, Accession NM\_030899). Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF323. LOC201965 (Accession XM\_114412) is another VGAM1510 host target gene. LOC201965 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201965, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201965 BINDING SITE, designated SEQ ID:42935, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52129] Another function of VGAM1510 is therefore inhibition of LOC201965 (Accession XM\_114412). Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201965. LOC51696 (Accession NM\_016217) is another VGAM1510 host target gene. LOC51696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51696 BINDING SITE, designated SEQ ID:18315, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52130] Another function of VGAM1510 is therefore inhibition of LOC51696 (Accession NM\_016217). Accordingly, utilities of VGAM1510 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC51696. LOC93349 (Accession NM\_138402) is another VGAM1510 host target gene. LOC93349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93349 BINDING SITE, designated SEQ ID:28771, to the nucleotide sequence of VGAM1510 RNA, herein designated VGAM RNA, also designated SEQ ID:4221.

[52131] Another function of VGAM1510 is therefore inhibition of LOC93349 (Accession NM\_138402). Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93349. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1511 (VGAM1511) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52132] VGAM1511 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1511 was detected is described hereinabove with reference to Figs. 1–8.

[52133] VGAM1511 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus V.

VGAM1511 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52134] VGAM1511 gene encodes a VGAM1511 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1511 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1511 precursor RNA is designated SEQ ID:1497, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1497 is located at position 4177 relative to the genome of Potato Virus V.

[52135] VGAM1511 precursor RNA folds onto itself, forming VGAM1511 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by



miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52136] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1511 folded precursor RNA into VGAM1511 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1511 RNA is designated SEQ ID:4222, and is provided hereinbelow with reference to the sequence listing part.

[52137] VGAM1511 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1511 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52138] VGAM1511 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1511 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1511 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52139] The complementary binding of VGAM1511 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1511 host target RNA into VGAM1511 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52140] It is appreciated that VGAM1511 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1511 host target genes. The mRNA of each one of this plurality of VGAM1511 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1511 RNA, herein designated VGAM RNA, and which when bound by VGAM1511 RNA causes inhibition of translation of respective one or more VGAM1511 host target proteins.

[52141] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1511 gene, herein designated VGAM GENE, on one or more VGAM1511 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52142] It is yet further appreciated that a function of VGAM1511 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1511 include diagnosis, prevention and treatment of viral infection by Potato Virus V. Specific functions, and accordingly utilities, of VGAM1511 correlate with, and may be deduced from, the identity of the host target genes which VGAM1511 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52143] Nucleotide sequences of the VGAM1511 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1511 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1511 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1511 are further described hereinbelow with reference to Table 1.

[52144] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1511 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1511 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52145] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1511 gene, herein designated VGAM is inhibition of expression of VGAM1511 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1511 correlate with, and may be deduced from, the identity of the target genes which VGAM1511 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52146] Natural Killer-tumor Recognition Sequence (NKTR, Accession NM\_005385) is a VGAM1511 host target gene. NKTR BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by NKTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NKTR BINDING SITE, designated SEQ ID:11864, to the nucleotide sequence of VGAM1511 RNA, herein designated VGAM RNA, also designated SEQ ID:4222.

[52147] A function of VGAM1511 is therefore inhibition of Natural Killer-tumor Recognition Sequence (NKTR, Accession NM\_005385), a gene which is involved in the function of nk cells. Accordingly, utilities of VGAM1511 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NKTR. The function of NKTR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM133. Oxytocin Receptor (OXTR, Accession NM\_000916) is another VGAM1511 host target gene. OXTR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by OXTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OXTR BINDING SITE,

designated SEQ ID:6621, to the nucleotide sequence of VGAM1511 RNA, herein designated VGAM RNA, also designated SEQ ID:4222.

[52148] Another function of VGAM1511 is therefore inhibition of Oxytocin Receptor (OXTR, Accession NM\_000916), a gene which induces inward ion currents. Accordingly, utilities of VGAM1511 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OXTR. The function of OXTR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM636. Cerebellin 1 Precursor (CBLN1, Accession NM\_004352) is another VGAM1511 host target gene. CBLN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBLN1 BINDING SITE, designated SEQ ID:10554, to the nucleotide sequence of VGAM1511 RNA, herein designated VGAM RNA, also designated SEQ ID:4222.

[52149] Another function of VGAM1511 is therefore inhibition of

Cerebellin 1 Precursor (CBLN1, Accession NM\_004352). Accordingly, utilities of VGAM1511 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBLN1. HSPC063 (Accession NM\_014155) is another VGAM1511 host target gene. HSPC063 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HSPC063, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC063 BINDING SITE, designated SEQ ID:15437, to the nucleotide sequence of VGAM1511 RNA, herein designated VGAM RNA, also designated SEQ ID:4222.

[52150] Another function of VGAM1511 is therefore inhibition of HSPC063 (Accession NM\_014155). Accordingly, utilities of VGAM1511 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC063. KIAA1871 (Accession XM\_028409) is another VGAM1511 host target gene. KIAA1871 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1871, corresponding to a HOST TARGET binding site such as BINDING SITE I,



BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1871 BINDING SITE, designated SEQ ID:30699, to the nucleotide sequence of VGAM1511 RNA, herein designated VGAM RNA, also designated SEQ ID:4222.

[52151] Another function of VGAM1511 is therefore inhibition of KIAA1871 (Accession XM\_028409). Accordingly, utilities of VGAM1511 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1871. Rab11-FIP2 (Accession NM\_014904) is another VGAM1511 host target gene. Rab11-FIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Rab11-FIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rab11-FIP2 BINDING SITE, designated SEQ ID:17098, to the nucleotide sequence of VGAM1511 RNA, herein designated VGAM RNA, also designated SEQ ID:4222.

[52152] Another function of VGAM1511 is therefore inhibition of Rab11-FIP2 (Accession NM\_014904). Accordingly, utilities of VGAM1511 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

Rab11–FIP2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1512 (VGAM1512) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52153] VGAM1512 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1512 was detected is described hereinabove with reference to Figs. 1–8.

[52154] VGAM1512 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Parsnip Yellow Fleck Virus. VGAM1512 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52155] VGAM1512 gene encodes a VGAM1512 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1512 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1512 precursor RNA is designated SEQ ID:1498, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1498 is located at position 7608 relative to the genome of Parsnip Yellow Fleck Virus.

- [52156] VGAM1512 precursor RNA folds onto itself, forming VGAM1512 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [52157] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1512 folded precursor RNA into VGAM1512 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1512 RNA is designated SEQ ID:4223, and is provided hereinbelow with reference to the sequence listing part.

[52158] VGAM1512 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1512 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52159] VGAM1512 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1512 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1512 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[52160] The complementary binding of VGAM1512 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1512 host target RNA into VGAM1512 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52161] It is appreciated that VGAM1512 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1512 host target genes. The mRNA of each one of this plurality of VGAM1512 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1512 RNA, herein designated VGAM RNA, and which when bound by VGAM1512 RNA causes

inhibition of translation of respective one or more VGAM1512 host target proteins.

[52162] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1512 gene, herein designated VGAM GENE, on one or more VGAM1512 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52163] It is yet further appreciated that a function of VGAM1512 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1512 include diagnosis, prevention and

treatment of viral infection by Parsnip Yellow Fleck Virus. Specific functions, and accordingly utilities, of VGAM1512 correlate with, and may be deduced from, the identity of the host target genes which VGAM1512 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52164] Nucleotide sequences of the VGAM1512 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1512 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1512 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1512 are further described hereinbelow with reference to Table 1.

[52165] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1512 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1512 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52166] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1512 gene, herein designated VGAM is inhibition of expression of VGAM1512 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1512 correlate with, and may be deduced from, the identity of the target genes which VGAM1512 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52167] Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM\_130436) is a VGAM1512 host target gene. DYRK1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DYRK1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE, designated SEQ ID:28184, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52168] A function of VGAM1512 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM\_130436), a gene which regulates cell proliferation and may be involved in brain development . Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK1A. The function of



DYRK1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42. Leucine Zipper Transcription Factor-like 1 (LZTFL1, Accession NM\_020347) is another VGAM1512 host target gene. LZTFL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LZTFL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTFL1 BINDING SITE, designated SEQ ID:21600, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52169] Another function of VGAM1512 is therefore inhibition of Leucine Zipper Transcription Factor-like 1 (LZTFL1, Accession NM\_020347). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTFL1. Syndecan 4 (amphiglycan, ryudocan) (SDC4, Accession NM\_002999) is another VGAM1512 host target gene. SDC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDC4, correspond-

ing to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC4 BINDING SITE, designated SEQ ID:8889, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52170] Another function of VGAM1512 is therefore inhibition of Syndecan 4 (amphiglycan, ryudocan) (SDC4, Accession NM\_002999), a gene which is a cell surface proteoglycan. Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC4. The function of SDC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Serum Deprivation Response (phosphatidylserine binding protein) (SDPR, Accession NM\_004657) is another VGAM1512 host target gene. SDPR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDPR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDPR BINDING SITE, designated SEQ ID:11024,

to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52171] Another function of VGAM1512 is therefore inhibition of Serum Deprivation Response (phosphatidylserine binding protein) (SDPR, Accession NM\_004657), a gene which substrate for protein\_kinase\_C ( assists in localizing PKC to invaginations of the plasma membrane. Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDPR. The function of SDPR has been established by previous studies. Gustincich et al. (1999) cloned SDPR from a human liver cDNA library using the murine homolog cloned by Gustincich and Schneider (1993) as probe. The SDPR cDNA encodes a deduced 425-amino acid peptide with a calculated molecular mass of 47.2 kD. The human and mouse proteins share 84% sequence identity; both contain a leucine zipper-like domain with 7 repeats and 2 putative protein kinase C phosphorylation sites. Northern blot analysis of various human tissues showed nearly ubiquitous expression of a 3.1-kb transcript, which was always coexpressed with a shorter transcript. Highest expression was detected in heart and lung. Gustincich et al. (1999) also found that SDPR mRNA was

detectable in asynchronously growing human fibroblast cells and was significantly upregulated after serum deprivation but not after density-dependent growth inhibition. Gustincich et al. (1999) determined that SDPR is the same as PS-p68, a phosphatidylserine-binding protein purified from human platelets by Burgener et al. (1990). SDPR localizes to the cytoplasm (Burgener et al., 1990; Gustincich et al., 1999). Using in vitro translation of histidine-tagged recombinant SDPR, Gustincich et al. (1999) found that SDPR is able to bind PS liposomes in a calcium-independent manner. Burgener et al. (1990) identified SDPR as the major PS-binding protein in platelets. They also found that SDPR was able to bind PKC in a cell-free assay in the presence of PS and calcium, resulting in SDPR phosphorylation.

[52172] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52173] Burgener, R.; Wolf, M.; Ganz, T.; Baggiolini, M. : Purification and characterization of a major phosphatidylserine-binding phosphoprotein from human platelets. *Biochem. J.* 269: 729-734, 1990. ; and

[52174] Gustincich, S.; Vatta, P.; Goruppi, S.; Wolf, M.; Saccone, S.;

Della Valle, G.; Baggiolini, M.; Schneider, C. : The human serum deprivation response gene (SDPR) maps to 2q32–q33 and cod.

[52175] Further studies establishing the function and utilities of SDPR are found in John Hopkins OMIM database record ID 606728, and in cited publications numbered 742–744 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Calpain 6 (CAPN6, Accession NM\_014289) is another VGAM1512 host target gene. CAPN6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPN6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN6 BINDING SITE, designated SEQ ID:15568, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52176] Another function of VGAM1512 is therefore inhibition of Calpain 6 (CAPN6, Accession NM\_014289). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN6. HERV-H LTR-associating 2 (HHLA2, Acces-

sion NM\_007072) is another VGAM1512 host target gene. HHLA2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HHLA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HHLA2 BINDING SITE, designated SEQ ID:13935, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52177] Another function of VGAM1512 is therefore inhibition of HERV-H LTR-associating 2 (HHLA2, Accession NM\_007072). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HHLA2. Integrin, Alpha 10 (ITGA10, Accession XM\_002097) is another VGAM1512 host target gene. ITGA10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ITGA10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA10 BINDING SITE, designated SEQ ID:29863, to the nucleotide sequence of

VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52178] Another function of VGAM1512 is therefore inhibition of Integrin, Alpha 10 (ITGA10, Accession XM\_002097). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA10. SIMRP7 (Accession XM\_166462) is another VGAM1512 host target gene. SIMRP7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIMRP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIMRP7 BINDING SITE, designated SEQ ID:44370, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52179] Another function of VGAM1512 is therefore inhibition of SIMRP7 (Accession XM\_166462). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIMRP7. LOC145497 (Accession XM\_085150) is another VGAM1512 host target gene. LOC145497 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC145497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145497 BINDING SITE, designated SEQ ID:37873, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52180] Another function of VGAM1512 is therefore inhibition of LOC145497 (Accession XM\_085150). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145497. LOC153469 (Accession XM\_087681) is another VGAM1512 host target gene. LOC153469 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153469, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153469 BINDING SITE, designated SEQ ID:39378, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52181] Another function of VGAM1512 is therefore inhibition of LOC153469 (Accession XM\_087681). Accordingly, utilities



of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153469. LOC220766 (Accession XM\_165471) is another VGAM1512 host target gene. LOC220766 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220766 BINDING SITE, designated SEQ ID:43654, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52182] Another function of VGAM1512 is therefore inhibition of LOC220766 (Accession XM\_165471). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220766. LOC221431 (Accession XM\_166380) is another VGAM1512 host target gene. LOC221431 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221431, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC221431 BINDING SITE, designated SEQ ID:44222, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52183] Another function of VGAM1512 is therefore inhibition of LOC221431 (Accession XM\_166380). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221431. LOC222787 (Accession XM\_169879) is another VGAM1512 host target gene. LOC222787 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222787, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222787 BINDING SITE, designated SEQ ID:45304, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52184] Another function of VGAM1512 is therefore inhibition of LOC222787 (Accession XM\_169879). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222787. LOC257396 (Accession XM\_173148) is another VGAM1512 host target gene. LOC257396 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257396, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257396 BINDING SITE, designated SEQ ID:46406, to the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, also designated SEQ ID:4223.

[52185] Another function of VGAM1512 is therefore inhibition of LOC257396 (Accession XM\_173148). Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257396. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1513 (VGAM1513) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52186] VGAM1513 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1513 was detected is described hereinabove with reference to Figs. 1-8.

[52187] VGAM1513 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Parsnip Yellow Fleck Virus. VGAM1513 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52188] VGAM1513 gene encodes a VGAM1513 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1513 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1513 precursor RNA is designated SEQ ID:1499, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1499 is located at position 3 relative to the genome of Parsnip Yellow Fleck Virus.

[52189] VGAM1513 precursor RNA folds onto itself, forming VGAM1513 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[52190] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1513 folded precursor RNA into VGAM1513 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM1513 RNA is designated SEQ ID:4224, and is provided hereinbelow with reference to the sequence listing part.

[52191] VGAM1513 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1513 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1513 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52192] VGAM1513 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1513 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1513 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1513 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1513 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52193] The complementary binding of VGAM1513 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1513 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1513 host target RNA into VGAM1513 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52194] It is appreciated that VGAM1513 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1513 host target genes. The mRNA of each one of this plurality of VGAM1513 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1513 RNA, herein designated VGAM RNA, and which when bound by VGAM1513 RNA causes inhibition of translation of respective one or more VGAM1513 host target proteins.

[52195] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1513 gene, herein designated VGAM GENE, on one or more VGAM1513 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52196] It is yet further appreciated that a function of VGAM1513 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1513 include diagnosis, prevention and treatment of viral infection by Parsnip Yellow Fleck Virus. Specific functions, and accordingly utilities, of VGAM1513 correlate with, and may be deduced from, the identity of the host target genes which VGAM1513 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52197] Nucleotide sequences of the VGAM1513 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1513 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1513 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, of VGAM1513 are further described hereinbelow with reference to Table 1.

[52198] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1513 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1513 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52199] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1513 gene, herein designated VGAM is inhibition of expression of VGAM1513 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1513 correlate with, and may be deduced from, the identity of the target genes which VGAM1513 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52200] UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 2 (B3GALT2, Accession NM\_003783) is a VGAM1513 host target gene. B3GALT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by B3GALT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT2 BINDING SITE, designated SEQ ID:9868, to the nucleotide sequence of VGAM1513 RNA, herein designated VGAM RNA, also designated SEQ ID:4224.

[52201] A function of VGAM1513 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 2 (B3GALT2, Accession NM\_003783). Accordingly, utilities of VGAM1513 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT2. DXS1283E (Accession XM\_047871) is another VGAM1513 host target gene. DXS1283E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DXS1283E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DXS1283E BINDING SITE, designated SEQ ID:35059, to the nucleotide sequence of VGAM1513 RNA, herein designated VGAM RNA, also designated SEQ ID:4224.

[52202] Another function of VGAM1513 is therefore inhibition of DXS1283E (Accession XM\_047871). Accordingly, utilities of VGAM1513 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with DXS1283E. DKFZp434N074 (Accession XM\_031481) is another VGAM1513 host target gene. DKFZp434N074 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp434N074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434N074 BINDING SITE, designated SEQ ID:31388, to the nucleotide sequence of VGAM1513 RNA, herein designated VGAM RNA, also designated SEQ ID:4224.

[52203] Another function of VGAM1513 is therefore inhibition of DKFZp434N074 (Accession XM\_031481). Accordingly, utilities of VGAM1513 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434N074. FLJ10759 (Accession NM\_018207) is another VGAM1513 host target gene. FLJ10759 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FLJ10759 BINDING SITE, designated SEQ ID:20098, to the nucleotide sequence of VGAM1513 RNA, herein designated VGAM RNA, also designated SEQ ID:4224.

[52204] Another function of VGAM1513 is therefore inhibition of FLJ10759 (Accession NM\_018207). Accordingly, utilities of VGAM1513 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10759. LOC153561 (Accession XM\_087708) is another VGAM1513 host target gene. LOC153561 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153561, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153561 BINDING SITE, designated SEQ ID:39400, to the nucleotide sequence of VGAM1513 RNA, herein designated VGAM RNA, also designated SEQ ID:4224.

[52205] Another function of VGAM1513 is therefore inhibition of LOC153561 (Accession XM\_087708). Accordingly, utilities of VGAM1513 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153561. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1514 (VGAM1514) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52206] VGAM1514 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1514 was detected is described hereinabove with reference to Figs. 1–8.

[52207] VGAM1514 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Parsnip Yellow Fleck Virus. VGAM1514 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52208] VGAM1514 gene encodes a VGAM1514 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1514 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1514 precursor RNA is designated SEQ ID:1500, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1500 is located at position 9392 relative to the

genome of Parsnip Yellow Fleck Virus.

[52209] VGAM1514 precursor RNA folds onto itself, forming VGAM1514 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52210] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1514 folded precursor RNA into VGAM1514 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1514 RNA is designated SEQ ID:4225, and is provided hereinbelow with reference to the sequence listing part.

[52211] VGAM1514 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1514 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[52212] VGAM1514 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1514 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1514 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52213] The complementary binding of VGAM1514 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1514 host target RNA into VGAM1514 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52214] It is appreciated that VGAM1514 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1514 host target genes. The mRNA of each one of this plurality of VGAM1514 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1514 RNA, herein designated VGAM RNA, and which when bound by VGAM1514 RNA causes inhibition of translation of respective one or more VGAM1514 host target proteins.



[52215] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1514 gene, herein designated VGAM GENE, on one or more VGAM1514 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52216] It is yet further appreciated that a function of VGAM1514 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of viral infection by Parsnip Yellow Fleck Virus. Specific functions, and accordingly utilities, of VGAM1514

correlate with, and may be deduced from, the identity of the host target genes which VGAM1514 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52217] Nucleotide sequences of the VGAM1514 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1514 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1514 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1514 are further described hereinbelow with reference to Table 1.

[52218] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1514 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1514 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52219] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1514 gene, herein designated VGAM is inhibition of expression of VGAM1514 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1514 correlate with, and may be deduced

from, the identity of the target genes which VGAM1514 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52220] Basonuclin (BNC, Accession NM\_001717) is a VGAM1514 host target gene. BNC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BNC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BNC BINDING SITE, designated SEQ ID:7450, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52221] A function of VGAM1514 is therefore inhibition of Basonuclin (BNC, Accession NM\_001717), a gene which plays a role in the maintenance of proliferative capacity and prevention of terminal differentiation of keratinocytes. Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BNC. The function of BNC has been established by previous studies. Basonuclin (BNC) is a protein found mainly in cells of the basal layer of stratified squamous epithelia. Tseng and Green (1992) isolated a

cDNA encoding this protein from mRNA of cultured human keratinocytes. The basonuclin cDNA encodes a 993-amino acid polypeptide that is located in the nucleus and contains 6 zinc finger motifs of the C2H2 class, as in known transcription factors. Basonuclin is expressed in cells that are able to undergo division but are not necessarily in the division cycle; the protein is not found in terminally differentiated cells (Tseng and Green, 1994). These properties suggested that basonuclin performs a transcriptional regulatory function related to promotion of keratinocyte growth or suppression of keratinocyte differentiation. Teumer et al. (1997) cloned and sequenced the basonuclin gene from a human genomic library. By analysis of human/rodent hybrid cells, they mapped it to chromosome 15. The transcription unit spans nearly 29 kb of sequence. The coding region is distributed over 5 exons and the 3 pairs of zinc fingers encoded by the last 2 exons. The 5-prime flanking sequence and first exon are unusually rich in GC content and in CpG dinucleotides. This sequence region contains numerous binding sites for the transcription factor Sp1 (OMIM Ref. No. 189906).

[52222] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

[52223] Tseng, H.; Green, H. : Basonuclin: a keratinocyte protein with multiple paired zinc fingers. Proc. Nat. Acad. Sci. 89: 10311–10315, 1992. ; and

[52224] Tseng, H.; Green, H. : Association of basonuclin with ability of keratinocytes to multiply and with absence of terminal differentiation. J. Cell Biol. 126: 495–506, 1994.

[52225] Further studies establishing the function and utilities of BNC are found in John Hopkins OMIM database record ID 601930, and in cited publications numbered 6253–6255 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Necdin Homolog (mouse) (NDN, Accession NM\_002487) is another VGAM1514 host target gene. NDN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDN BINDING SITE, designated SEQ ID:8312, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52226] Another function of VGAM1514 is therefore inhibition of

Necdin Homolog (mouse) (NDN, Accession NM\_002487), a gene which facilitates the entry of the cell into cell cycle arrest. Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDN. The function of NDN has been established by previous studies. Reasoning that additional imprinted genes may lie within the Prader-Willi syndrome (PWS; 176270) deletion interval 15q11-q13, MacDonald and Wevrick (1997) searched for transcribed sequences in the region between the 2 imprinted genes ZNF127 (MKRN3; 603856) and SNRPN (OMIM Ref. No. 182279). An expressed sequence tag (EST) showed 99% sequence identity to the 3-prime end of a GenBank sequence (OMIM Ref. No. U35139), defined as 'a human necdin-related protein mRNA.' They concluded that the putative necdin-encoding gene is a single locus in proximal 15q, as determined by radiation hybrid mapping, localization of the appropriate PCR-amplified fragments to overlapping YACs, and absence in other YACs from the PWS deletion region. Mouse necdin (gene locus Ndn) was originally identified by Maruyama et al. (1991) as a protein encoded by a neural differentiation-specific mRNA, derived from embryonal carcinoma cells. The necdin protein

is localized to the nuclei of postmitotic neurons and is expressed in almost all postmitotic neurons in the CNS from the beginning of neural differentiation and into adult life. The *Ndn* locus is present as a single exon in the mouse genome and was mapped to mouse chromosome 7 in a region of conserved synteny with human 15q11–q13 by MacDonald and Wevrick (1997) using genetic mapping in an interspecific backcross panel. They demonstrated, furthermore, that expression of the *Ndn* mouse gene and the *NDN* human gene is limited to the paternal allele, with highest levels of expression in brain and placenta. Consistent with the observation that imprinted genes have few and small introns (Hurst et al., 1996), human *NDN* is contained within a single exon, like its mouse ortholog. They suggested that loss of *necdin* gene expression may contribute to the disorder of brain development in individuals with PWS. Jay et al. (1997) likewise cloned a human cDNA with close similarities to the mouse *necdin* gene. They mapped the *NDN* gene to 15q11–q13 by fluorescence in situ hybridization (FISH), and confirmed the location by PCR analysis of DNA extracted from a panel of hamster/human somatic cell hybrids. Both approaches suggested that the *NDN* gene maps to 15q11–q13 but that a homologous

gene or pseudogene maps to 12q21. Jay et al. (1997) also mapped NDN by hybridization to a YAC contig covering the PWS critical region. They suggested that NDN is located approximately 100 kb distal to ZNF127 and 1 to 1.5 Mb proximal to SNRPN. NDN displayed several characteristics of an imprinted locus, including allelic DNA methylation and an asynchronous DNA replication. Jay et al. (1997) found a complete lack of NDN expression in PWS brain and fibroblasts, indicating that the gene is expressed exclusively from the paternal allele in these tissues and suggesting a possible role of this gene in PWS.

[52227] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52228] Hurst, L. D.; McVean, G.; Moore, T. : Imprinted genes have few and small introns. (Letter) Nature Genet. 12: 234–237, 1996. ; and

[52229] Jay, P.; Rougeulle, C.; Massacrier, A.; Moncla, A.; Mattei, M.–G.; Malzac, P.; Roeckel, N.; Taviaux, S.; Lefranc, J.–L. B.; Cau, P.; Berta, P.; Lalande, M.; Muscatelli, F. : The human n.

[52230] Further studies establishing the function and utilities of NDN are found in John Hopkins OMIM database record ID



602117, and in cited publications numbered 8921–8930 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Oligodendrocyte Lineage Transcription Factor 2 (OLIG2, Accession NM\_005806) is another VGAM1514 host target gene. OLIG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OLIG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OLIG2 BINDING SITE, designated SEQ ID:12382, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52231] Another function of VGAM1514 is therefore inhibition of Oligodendrocyte Lineage Transcription Factor 2 (OLIG2, Accession NM\_005806), a gene which may bind DNA and contains a helix–loop–helix DNA–binding domain. Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OLIG2. The function of OLIG2 has been established by previous studies. The oligodendrocyte lineage transcription factors OLIG1 (OMIM Ref. No. 606385)

and OLIG2, originally identified in rodents, encode basic helix–loop–helix transcription factors. In the rodent central nervous system, they are expressed exclusively in oligodendrocytes and oligodendrocyte precursors (Lu et al., 2000; Zhou et al., 2000). Pursuing the suggestion that novel molecular markers might be found among factors that have roles in glial development (Raff et al., 1983), Lu et al. (2001) found that the human OLIG1/2 genes are expressed strongly in oligodendroglioma, contrasting absent or low expression in astrocytoma. Their study provided evidence that neoplastic cells of oligodendroglioma resemble oligodendrocytes or their progenitor cells and may derive from cells of this lineage. Animal model experiments lend further support to the function of OLIG2. In Olig1/2 double–mutant mice, Zhou and Anderson (2002) found that motoneurons were largely eliminated, and oligodendrocyte differentiation was abolished. Lineage tracing data suggested that Olig1/2  $-/-$  pMN progenitors instead generated V2 interneurons and then astrocytes. This apparent conversion likely reflects independent roles for OLIG1/2 in specifying motoneuron and oligodendrocyte fates. OLIG genes therefore couple neuronal and glial subtype specification, unlike proneural bHLH factors that

control the neuron versus glia decision. The authors concluded that, in the spinal cord, OLIG and proneural genes comprise a combinatorial code for the specification of neurons, astrocytes, and oligodendrocytes, the 3 fundamental cell types of the central nervous system.

[52232] It is appreciated that the abovementioned animal model for OLIG2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[52233] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52234] Lu, Q. R.; Park, J. K.; Noll, E.; Chan, J. A.; Alberta, J.; Yuk, D.; Alzamora, M. G.; Louis, D. N.; Stiles, C. D.; Rowitch, D. H.; Black, P. M. : Oligodendrocyte lineage genes (OLIG) as molecular markers for human glial brain tumors. Proc. Nat. Acad. Sci. 98: 10851–10856, 2001. ; and

[52235] Zhou, Q.; Anderson, D. J. : The bHLH transcription factors OLIG2 and OLIG1 couple neuronal and glial subtype specification. Cell 109: 61–73, 2002.

[52236] Further studies establishing the function and utilities of OLIG2 are found in John Hopkins OMIM database record ID 606386, and in cited publications numbered 647 and

6585–6589 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAS Guanyl Releasing Protein 1 (calcium and DAG–regulated) (RASGRP1, Accession NM\_005739) is another VGAM1514 host target gene. RASGRP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RASGRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASGRP1 BINDING SITE, designated SEQ ID:12302, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52237] Another function of VGAM1514 is therefore inhibition of RAS Guanyl Releasing Protein 1 (calcium and DAG–regulated) (RASGRP1, Accession NM\_005739). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASGRP1. SNL (Accession NM\_003088) is another VGAM1514 host target gene. SNL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND–

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNL BINDING SITE, designated SEQ ID:9064, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52238] Another function of VGAM1514 is therefore inhibition of SNL (Accession NM\_003088), a gene which organizes filamentous actin into bundles with a minimum of 4.1:1 actin/fascin ratio. Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNL. The function of SNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675. Wingless-type MMTV Integration Site Family, Member 5A (WNT5A, Accession NM\_003392) is another VGAM1514 host target gene. WNT5A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by WNT5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT5A BINDING SITE, designated SEQ ID:9429, to the nucleotide se-

quence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52239] Another function of VGAM1514 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 5A (WNT5A, Accession NM\_003392), a gene which is a ligand for members of the frizzled family of seven transmembrane receptors and is probably a developmental protein. Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT5A. The function of WNT5A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM996. Butyrophilin, Subfamily 2, Member A2 (BTN2A2, Accession NM\_006995) is another VGAM1514 host target gene. BTN2A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN2A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN2A2 BINDING SITE, designated SEQ ID:13859, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ

ID:4225.

[52240] Another function of VGAM1514 is therefore inhibition of Butyrophilin, Subfamily 2, Member A2 (BTN2A2, Accession NM\_006995). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN2A2. Chromosome 17 Open Reading Frame 1A (C17orf1A, Accession NM\_006382) is another VGAM1514 host target gene. C17orf1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C17orf1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf1A BINDING SITE, designated SEQ ID:13086, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52241] Another function of VGAM1514 is therefore inhibition of Chromosome 17 Open Reading Frame 1A (C17orf1A, Accession NM\_006382). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf1A. Calcium-binding tyrosine-(Y)-phosphorylation Regulated

(fibrousheathin 2) (CABYR, Accession NM\_012189) is another VGAM1514 host target gene. CABYR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CABYR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CABYR BINDING SITE, designated SEQ ID:14477, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52242] Another function of VGAM1514 is therefore inhibition of Calcium-binding tyrosine-(Y)-phosphorylation Regulated (fibrousheathin 2) (CABYR, Accession NM\_012189). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CABYR. CD36L1 (Accession NM\_005505) is another VGAM1514 host target gene. CD36L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CD36L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD36L1 BINDING SITE, designated SEQ ID:12019, to the



nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52243] Another function of VGAM1514 is therefore inhibition of CD36L1 (Accession NM\_005505). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD36L1. CGI-01 (Accession NM\_015935) is another VGAM1514 host target gene. CGI-01 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGI-01, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGI-01 BINDING SITE, designated SEQ ID:18055, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52244] Another function of VGAM1514 is therefore inhibition of CGI-01 (Accession NM\_015935). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGI-01. DKFZp434C0328 (Accession NM\_017577) is another VGAM1514 host target gene. DKFZp434C0328 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by DKFZp434C0328, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434C0328 BINDING SITE, designated SEQ ID:19014, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52245] Another function of VGAM1514 is therefore inhibition of DKFZp434C0328 (Accession NM\_017577). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434C0328. FLJ11588 (Accession NM\_024603) is another VGAM1514 host target gene. FLJ11588 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11588, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11588 BINDING SITE, designated SEQ ID:23853, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52246] Another function of VGAM1514 is therefore inhibition of

FLJ11588 (Accession NM\_024603). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11588. FLJ12838 (Accession NM\_024641) is another VGAM1514 host target gene. FLJ12838 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12838, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12838 BINDING SITE, designated SEQ ID:23923, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52247] Another function of VGAM1514 is therefore inhibition of FLJ12838 (Accession NM\_024641). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12838. FLJ20400 (Accession XM\_039306) is another VGAM1514 host target gene. FLJ20400 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20400, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of FLJ20400 BINDING SITE, designated SEQ ID:33044, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52248] Another function of VGAM1514 is therefore inhibition of FLJ20400 (Accession XM\_039306). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20400. KIAA0638 (Accession XM\_051489) is another VGAM1514 host target gene. KIAA0638 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0638, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0638 BINDING SITE, designated SEQ ID:35846, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52249] Another function of VGAM1514 is therefore inhibition of KIAA0638 (Accession XM\_051489). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0638. KIAA0894 (Accession NM\_014896) is another

VGAM1514 host target gene. KIAA0894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0894 BINDING SITE, designated SEQ ID:17057, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52250] Another function of VGAM1514 is therefore inhibition of KIAA0894 (Accession NM\_014896). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0894. KIAA1204 (Accession XM\_045011) is another VGAM1514 host target gene. KIAA1204 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1204, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1204 BINDING SITE, designated SEQ ID:34315, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52251] Another function of VGAM1514 is therefore inhibition of KIAA1204 (Accession XM\_045011). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1204. Leucine-rich Repeat LGI Family, Member 4 (LGI4, Accession NM\_139284) is another VGAM1514 host target gene. LGI4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LGI4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGI4 BINDING SITE, designated SEQ ID:29288, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52252] Another function of VGAM1514 is therefore inhibition of Leucine-rich Repeat LGI Family, Member 4 (LGI4, Accession NM\_139284). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGI4. MGC4172 (Accession NM\_024308) is another VGAM1514 host target gene. MGC4172 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by MGC4172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4172 BINDING SITE, designated SEQ ID:23598, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52253] Another function of VGAM1514 is therefore inhibition of MGC4172 (Accession NM\_024308). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4172. MIDORI (Accession XM\_057651) is another VGAM1514 host target gene. MIDORI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIDORI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIDORI BINDING SITE, designated SEQ ID:36529, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52254] Another function of VGAM1514 is therefore inhibition of MIDORI (Accession XM\_057651). Accordingly, utilities of

VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MI-DORI. ZF5128 (Accession NM\_014347) is another VGAM1514 host target gene. ZF5128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZF5128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZF5128 BINDING SITE, designated SEQ ID:15671, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52255] Another function of VGAM1514 is therefore inhibition of ZF5128 (Accession NM\_014347). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZF5128. LOC145989 (Accession XM\_004815) is another VGAM1514 host target gene. LOC145989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of



LOC145989 BINDING SITE, designated SEQ ID:29952, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52256] Another function of VGAM1514 is therefore inhibition of LOC145989 (Accession XM\_004815). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145989. LOC148195 (Accession XM\_097419) is another VGAM1514 host target gene. LOC148195 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148195 BINDING SITE, designated SEQ ID:40877, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52257] Another function of VGAM1514 is therefore inhibition of LOC148195 (Accession XM\_097419). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148195. LOC158714 (Accession XM\_088650) is another VGAM1514 host target gene. LOC158714 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158714 BINDING SITE, designated SEQ ID:39885, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52258] Another function of VGAM1514 is therefore inhibition of LOC158714 (Accession XM\_088650). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158714. LOC257407 (Accession XM\_173078) is another VGAM1514 host target gene. LOC257407 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257407 BINDING SITE, designated SEQ ID:46336, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52259] Another function of VGAM1514 is therefore inhibition of

LOC257407 (Accession XM\_173078). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257407. LOC91115 (Accession XM\_036218) is another VGAM1514 host target gene. LOC91115 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91115, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91115 BINDING SITE, designated SEQ ID:32397, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52260] Another function of VGAM1514 is therefore inhibition of LOC91115 (Accession XM\_036218). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91115. LOC92305 (Accession NM\_138385) is another VGAM1514 host target gene. LOC92305 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC92305 BINDING SITE, designated SEQ ID:28759, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52261] Another function of VGAM1514 is therefore inhibition of LOC92305 (Accession NM\_138385). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92305. LOC92997 (Accession XM\_048690) is another VGAM1514 host target gene. LOC92997 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92997, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92997 BINDING SITE, designated SEQ ID:35221, to the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, also designated SEQ ID:4225.

[52262] Another function of VGAM1514 is therefore inhibition of LOC92997 (Accession XM\_048690). Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92997. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1515 (VGAM1515) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52263] VGAM1515 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1515 was detected is described hereinabove with reference to Figs. 1–8.

[52264] VGAM1515 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Parsnip Yellow Fleck Virus. VGAM1515 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52265] VGAM1515 gene encodes a VGAM1515 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1515 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1515 precursor RNA is designated SEQ ID:1501, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1501 is located at position 2895 relative to the genome of Parsnip Yellow Fleck Virus.

[52266] VGAM1515 precursor RNA folds onto itself, forming VGAM1515 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52267] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1515 folded precursor RNA into VGAM1515 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1515 RNA is designated SEQ ID:4226, and is provided hereinbelow with reference to the sequence listing part.

[52268] VGAM1515 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1515 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1515 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52269] VGAM1515 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1515 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1515 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1515 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1515 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52270] The complementary binding of VGAM1515 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1515 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1515 host target RNA into VGAM1515 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52271] It is appreciated that VGAM1515 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1515 host target genes. The mRNA of each one of this plurality of VGAM1515 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1515 RNA, herein designated VGAM RNA, and which when bound by VGAM1515 RNA causes inhibition of translation of respective one or more



VGAM1515 host target proteins.

[52272] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1515 gene, herein designated VGAM GENE, on one or more VGAM1515 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52273] It is yet further appreciated that a function of VGAM1515 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1515 include diagnosis, prevention and treatment of viral infection by Parsnip Yellow Fleck Virus.

Specific functions, and accordingly utilities, of VGAM1515 correlate with, and may be deduced from, the identity of the host target genes which VGAM1515 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52274] Nucleotide sequences of the VGAM1515 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1515 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1515 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1515 are further described hereinbelow with reference to Table 1.

[52275] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1515 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1515 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52276] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1515 gene, herein designated VGAM is inhibition of expression of VGAM1515 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1515 correlate with, and may be deduced from, the identity of the target genes which VGAM1515 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52277] Junctional Adhesion Molecule 3 (JAM3, Accession NM\_032801) is a VGAM1515 host target gene. JAM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JAM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAM3 BINDING SITE, designated SEQ ID:26557, to the nucleotide sequence of VGAM1515 RNA, herein designated VGAM RNA, also designated SEQ ID:4226.

[52278] A function of VGAM1515 is therefore inhibition of Junctional Adhesion Molecule 3 (JAM3, Accession NM\_032801), a gene which is a member of the junctional adhesion molecule protein family. Accordingly, utilities of VGAM1515 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAM3. The function of JAM3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM200. Matrilin 3 (MATN3, Accession NM\_002381) is another VGAM1515 host target gene. MATN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MATN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MATN3 BINDING SITE, designated SEQ ID:8198, to the nucleotide sequence of VGAM1515 RNA, herein designated VGAM RNA, also designated SEQ ID:4226.

[52279] Another function of VGAM1515 is therefore inhibition of Matrilin 3 (MATN3, Accession NM\_002381). Accordingly, utilities of VGAM1515 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MATN3. Zinc Finger Protein 278 (ZNF278, Accession NM\_014323) is another VGAM1515 host target gene. ZNF278 BINDING SITE1 through ZNF278 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ZNF278, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF278 BINDING SITE1 through ZNF278 BINDING SITE3, design-

nated SEQ ID:15623, SEQ ID:25772 and SEQ ID:25781 respectively, to the nucleotide sequence of VGAM1515 RNA, herein designated VGAM RNA, also designated SEQ ID:4226.

[52280] Another function of VGAM1515 is therefore inhibition of Zinc Finger Protein 278 (ZNF278, Accession NM\_014323), a gene which represses basal transcription as well as RNF4-mediated activation. Accordingly, utilities of VGAM1515 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF278. The function of ZNF278 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM414.HSMPP8 (Accession XM\_167894) is another VGAM1515 host target gene. HSMPP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSMPP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSMPP8 BINDING SITE, designated SEQ ID:44902, to the nucleotide sequence of VGAM1515 RNA, herein designated VGAM RNA, also designated SEQ ID:4226.

[52281] Another function of VGAM1515 is therefore inhibition of HSMPP8 (Accession XM\_167894). Accordingly, utilities of VGAM1515 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSMPP8. TERF1 (TRF1)–interacting Nuclear Factor 2 (TINF2, Accession NM\_012461) is another VGAM1515 host target gene. TINF2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TINF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TINF2 BINDING SITE, designated SEQ ID:14834, to the nucleotide sequence of VGAM1515 RNA, herein designated VGAM RNA, also designated SEQ ID:4226.

[52282] Another function of VGAM1515 is therefore inhibition of TERF1 (TRF1)–interacting Nuclear Factor 2 (TINF2, Accession NM\_012461). Accordingly, utilities of VGAM1515 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TINF2. LOC154386 (Accession XM\_087920) is another VGAM1515 host target gene. LOC154386 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded

by LOC154386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154386 BINDING SITE, designated SEQ ID:39473, to the nucleotide sequence of VGAM1515 RNA, herein designated VGAM RNA, also designated SEQ ID:4226.

[52283] Another function of VGAM1515 is therefore inhibition of LOC154386 (Accession XM\_087920). Accordingly, utilities of VGAM1515 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154386. LOC256158 (Accession XM\_175125) is another VGAM1515 host target gene. LOC256158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE, designated SEQ ID:46637, to the nucleotide sequence of VGAM1515 RNA, herein designated VGAM RNA, also designated SEQ ID:4226.

[52284] Another function of VGAM1515 is therefore inhibition of LOC256158 (Accession XM\_175125). Accordingly, utilities

of VGAM1515 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256158. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1516 (VGAM1516) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52285] VGAM1516 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1516 was detected is described hereinabove with reference to Figs. 1-8.

[52286] VGAM1516 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Parsnip Yellow Fleck Virus. VGAM1516 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52287] VGAM1516 gene encodes a VGAM1516 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1516 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-



cleotide sequence of VGAM1516 precursor RNA is designated SEQ ID:1502, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1502 is located at position 1828 relative to the genome of Parsnip Yellow Fleck Virus.

[52288] VGAM1516 precursor RNA folds onto itself, forming VGAM1516 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52289] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1516 folded precursor RNA into VGAM1516 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM1516 RNA is designated SEQ ID:4227, and

is provided hereinbelow with reference to the sequence listing part.

[52290] VGAM1516 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1516 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[52291] VGAM1516 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1516 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1516 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52292] The complementary binding of VGAM1516 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1516 host target RNA into VGAM1516 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52293] It is appreciated that VGAM1516 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1516 host target genes. The mRNA of each one of this plurality of VGAM1516 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1516 RNA, herein designated VGAM RNA, and which when bound by VGAM1516 RNA causes inhibition of translation of respective one or more VGAM1516 host target proteins.

[52294] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1516 gene, herein designated VGAM GENE, on one or more VGAM1516 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52295] It is yet further appreciated that a function of VGAM1516 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment of viral infection by Parsnip Yellow Fleck Virus. Specific functions, and accordingly utilities, of VGAM1516 correlate with, and may be deduced from, the identity of the host target genes which VGAM1516 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52296] Nucleotide sequences of the VGAM1516 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1516 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1516 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1516 are further described hereinbelow with reference to Table 1.

[52297] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1516 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1516 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52298] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1516 gene, herein designated VGAM is inhibition of expression of VGAM1516 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1516 correlate with, and may be deduced from, the identity of the target genes which VGAM1516 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52299] Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM\_004621) is a VGAM1516 host target gene. TRPC6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC6 BINDING SITE, designated SEQ ID:10979, to the nucleotide sequence of VGAM1516 RNA, herein designated VGAM RNA, also designated SEQ ID:4227.

[52300] A function of VGAM1516 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM\_004621), a gene which has calcium channel activity. Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with TRPC6. The function of TRPC6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Ankyrin Repeat and SOCS Box-containing 13 (ASB13, Accession NM\_024701) is another VGAM1516 host target gene. ASB13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ASB13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASB13 BINDING SITE, designated SEQ ID:24014, to the nucleotide sequence of VGAM1516 RNA, herein designated VGAM RNA, also designated SEQ ID:4227.

[52301] Another function of VGAM1516 is therefore inhibition of Ankyrin Repeat and SOCS Box-containing 13 (ASB13, Accession NM\_024701). Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASB13. CUB and Sushi Multiple Domains 1 (CSMD1, Accession NM\_033225) is another VGAM1516 host target gene. CSMD1 BINDING SITE1 and CSMD1 BINDING SITE2 are HOST TARGET bind-

ing sites found in untranslated regions of mRNA encoded by CSMD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSMD1 BINDING SITE1 and CSMD1 BINDING SITE2, designated SEQ ID:27071 and SEQ ID:36194 respectively, to the nucleotide sequence of VGAM1516 RNA, herein designated VGAM RNA, also designated SEQ ID:4227.

[52302] Another function of VGAM1516 is therefore inhibition of CUB and Sushi Multiple Domains 1 (CSMD1, Accession NM\_033225). Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSMD1. Hairy/enhancer-of-split Related with YRPW Motif 2 (HEY2, Accession NM\_012259) is another VGAM1516 host target gene. HEY2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HEY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEY2 BINDING SITE, designated SEQ ID:14566, to the nucleotide sequence of VGAM1516 RNA, herein



designated VGAM RNA, also designated SEQ ID:4227.

[52303] Another function of VGAM1516 is therefore inhibition of Hairy/enhancer-of-split Related with YRPW Motif 2 (HEY2, Accession NM\_012259). Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEY2. KIAA1944 (Accession XM\_062545) is another VGAM1516 host target gene. KIAA1944 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1944, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1944 BINDING SITE, designated SEQ ID:37230, to the nucleotide sequence of VGAM1516 RNA, herein designated VGAM RNA, also designated SEQ ID:4227.

[52304] Another function of VGAM1516 is therefore inhibition of KIAA1944 (Accession XM\_062545). Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1944. KIAA1956 (Accession XM\_085836) is another VGAM1516 host target gene. KIAA1956 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1956, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1956 BINDING SITE, designated SEQ ID:38362, to the nucleotide sequence of VGAM1516 RNA, herein designated VGAM RNA, also designated SEQ ID:4227.

[52305] Another function of VGAM1516 is therefore inhibition of KIAA1956 (Accession XM\_085836). Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1956. Protein Phosphatase 4, Regulatory Subunit 2 (PPP4R2, Accession NM\_019853) is another VGAM1516 host target gene. PPP4R2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPP4R2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP4R2 BINDING SITE, designated SEQ ID:21257, to the nucleotide sequence of VGAM1516 RNA, herein designated VGAM RNA, also designated SEQ ID:4227.

[52306] Another function of VGAM1516 is therefore inhibition of

Protein Phosphatase 4, Regulatory Subunit 2 (PPP4R2, Accession NM\_019853). Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP4R2.

LOC155438 (Accession XM\_098722) is another VGAM1516 host target gene. LOC155438 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155438 BINDING SITE, designated SEQ ID:41769, to the nucleotide sequence of VGAM1516 RNA, herein designated VGAM RNA, also designated SEQ ID:4227.

[52307] Another function of VGAM1516 is therefore inhibition of LOC155438 (Accession XM\_098722). Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155438. LOC200854 (Accession XM\_113396) is another VGAM1516 host target gene. LOC200854 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200854, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200854 BINDING SITE, designated SEQ ID:42253, to the nucleotide sequence of VGAM1516 RNA, herein designated VGAM RNA, also designated SEQ ID:4227.

[52308] Another function of VGAM1516 is therefore inhibition of LOC200854 (Accession XM\_113396). Accordingly, utilities of VGAM1516 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200854. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1517 (VGAM1517) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52309] VGAM1517 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1517 was detected is described hereinabove with reference to Figs. 1-8.

[52310] VGAM1517 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pea Seed-borne Mosaic Virus. VGAM1517 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52311] VGAM1517 gene encodes a VGAM1517 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1517 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1517 precursor RNA is designated SEQ ID:1503, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1503 is located at position 6741 relative to the genome of Pea Seed-borne Mosaic Virus.

[52312] VGAM1517 precursor RNA folds onto itself, forming VGAM1517 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52313] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1517 folded precursor RNA into VGAM1517

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1517 RNA is designated SEQ ID:4228, and is provided hereinbelow with reference to the sequence listing part.

[52314] VGAM1517 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1517 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1517 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52315] VGAM1517 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1517 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1517 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1517 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1517 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52316] The complementary binding of VGAM1517 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1517 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1517 host target RNA into VGAM1517 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[52317] It is appreciated that VGAM1517 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1517 host target genes. The mRNA of each one of this plurality of VGAM1517 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1517 RNA, herein designated VGAM RNA, and which when bound by VGAM1517 RNA causes inhibition of translation of respective one or more VGAM1517 host target proteins.

[52318] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1517 gene, herein designated VGAM GENE, on one or more VGAM1517 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52319] It is yet further appreciated that a function of VGAM1517 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1517 include diagnosis, prevention and treatment of viral infection by Pea Seed-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1517 correlate with, and may be deduced from, the identity of the host target genes which VGAM1517 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52320] Nucleotide sequences of the VGAM1517 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1517 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1517 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1517 are further described hereinbelow with reference to Table 1.

[52321] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1517 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1517 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52322] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1517 gene, herein designated VGAM is inhibition of expression of VGAM1517 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1517 correlate with, and may be deduced from, the identity of the target genes which VGAM1517 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52323] Keratin 16 (focal non-epidermolytic palmoplantar keratoderma) (KRT16, Accession XM\_170845) is a VGAM1517 host target gene. KRT16 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KRT16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KRT16 BINDING SITE, designated SEQ ID:45627, to the nucleotide sequence of

VGAM1517 RNA, herein designated VGAM RNA, also designated SEQ ID:4228.

[52324] A function of VGAM1517 is therefore inhibition of Keratin 16 (focal non-epidermolytic palmoplantar keratoderma) (KRT16, Accession XM\_170845). Accordingly, utilities of VGAM1517 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KRT16. MGC3248 (Accession NM\_032486) is another VGAM1517 host target gene. MGC3248 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3248 BINDING SITE, designated SEQ ID:26234, to the nucleotide sequence of VGAM1517 RNA, herein designated VGAM RNA, also designated SEQ ID:4228.

[52325] Another function of VGAM1517 is therefore inhibition of MGC3248 (Accession NM\_032486). Accordingly, utilities of VGAM1517 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3248. LOC146515 (Accession XM\_085493) is another VGAM1517 host target gene. LOC146515 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146515 BINDING SITE, designated SEQ ID:38192, to the nucleotide sequence of VGAM1517 RNA, herein designated VGAM RNA, also designated SEQ ID:4228.

[52326] Another function of VGAM1517 is therefore inhibition of LOC146515 (Accession XM\_085493). Accordingly, utilities of VGAM1517 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146515. LOC158301 (Accession XM\_088543) is another VGAM1517 host target gene. LOC158301 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC158301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158301 BINDING SITE, designated SEQ ID:39809, to the nucleotide sequence of VGAM1517 RNA, herein designated VGAM RNA, also designated SEQ ID:4228.

[52327] Another function of VGAM1517 is therefore inhibition of

LOC158301 (Accession XM\_088543). Accordingly, utilities of VGAM1517 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158301. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1518 (VGAM1518) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52328] VGAM1518 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1518 was detected is described hereinabove with reference to Figs. 1-8.

[52329] VGAM1518 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pea Seed-borne Mosaic Virus. VGAM1518 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52330] VGAM1518 gene encodes a VGAM1518 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1518 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1518 precursor RNA is designated SEQ ID:1504, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1504 is located at position 9398 relative to the genome of Pea Seed-borne Mosaic Virus.

- [52331] VGAM1518 precursor RNA folds onto itself, forming VGAM1518 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [52332] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1518 folded precursor RNA into VGAM1518 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide se-

quence of VGAM1518 RNA is designated SEQ ID:4229, and is provided hereinbelow with reference to the sequence listing part.

[52333] VGAM1518 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1518 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1518 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52334] VGAM1518 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1518 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1518 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1518 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1518 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[52335] The complementary binding of VGAM1518 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1518 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1518 host target RNA into VGAM1518 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52336] It is appreciated that VGAM1518 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1518 host target genes. The mRNA of each one of this plurality of VGAM1518 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1518 RNA, herein designated VGAM RNA, and which when bound by VGAM1518 RNA causes inhibition of translation of respective one or more VGAM1518 host target proteins.

[52337] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1518 gene, herein designated VGAM GENE, on one or more VGAM1518 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52338] It is yet further appreciated that a function of VGAM1518

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1518 include diagnosis, prevention and treatment of viral infection by Pea Seed-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1518 correlate with, and may be deduced from, the identity of the host target genes which VGAM1518 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52339] Nucleotide sequences of the VGAM1518 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1518 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1518 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1518 are further described hereinbelow with reference to Table 1.

[52340] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1518 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1518 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52341] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1518 gene, herein designated VGAM is inhibition of expression of VGAM1518 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1518 correlate with, and may be deduced from, the identity of the target genes which VGAM1518 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52342] DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM\_006892) is a VGAM1518 host target gene. DNMT3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNMT3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT3B BINDING SITE, designated SEQ ID:13761, to the nucleotide sequence of VGAM1518 RNA, herein designated VGAM RNA, also designated SEQ ID:4229.

[52343] A function of VGAM1518 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM\_006892), a gene which is required for genome wide de novo methylation. Accordingly, utilities of

VGAM1518 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT3B. The function of DNMT3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM280. Sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase) (SIAT8C, Accession NM\_015879) is another VGAM1518 host target gene. SIAT8C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SIAT8C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT8C BINDING SITE, designated SEQ ID:18025, to the nucleotide sequence of VGAM1518 RNA, herein designated VGAM RNA, also designated SEQ ID:4229.

[52344] Another function of VGAM1518 is therefore inhibition of Sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase) (SIAT8C, Accession NM\_015879). Accordingly, utilities of VGAM1518 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT8C. LOC149301 (Accession

XM\_086480) is another VGAM1518 host target gene.

LOC149301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149301 BINDING SITE, designated SEQ ID:38691, to the nucleotide sequence of VGAM1518 RNA, herein designated VGAM RNA, also designated SEQ ID:4229.

[52345] Another function of VGAM1518 is therefore inhibition of LOC149301 (Accession XM\_086480). Accordingly, utilities of VGAM1518 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149301. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1519 (VGAM1519) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52346] VGAM1519 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1519 was detected is described hereinabove with reference to Figs. 1–8.

[52347] VGAM1519 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pea Seed-borne Mosaic Virus. VGAM1519 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52348] VGAM1519 gene encodes a VGAM1519 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1519 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1519 precursor RNA is designated SEQ ID:1505, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1505 is located at position 3823 relative to the genome of Pea Seed-borne Mosaic Virus.

[52349] VGAM1519 precursor RNA folds onto itself, forming VGAM1519 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52350] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1519 folded precursor RNA into VGAM1519 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1519 RNA is designated SEQ ID:4230, and is provided hereinbelow with reference to the sequence listing part.

[52351] VGAM1519 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1519 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1519 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52352] VGAM1519 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1519 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1519 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1519 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1519 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[52353] The complementary binding of VGAM1519 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM1519 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1519 host target RNA into VGAM1519 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52354] It is appreciated that VGAM1519 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1519 host target genes. The mRNA of each one of this plurality of VGAM1519 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1519 RNA, herein designated VGAM RNA, and which when bound by VGAM1519 RNA causes inhibition of translation of respective one or more VGAM1519 host target proteins.

[52355] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1519 gene, herein designated VGAM GENE, on one or more VGAM1519 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52356] It is yet further appreciated that a function of VGAM1519 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of viral infection by Pea Seed-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1519 correlate with, and may be deduced from, the identity of the host target genes which VGAM1519 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52357] Nucleotide sequences of the VGAM1519 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1519 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1519 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1519 are further described hereinbelow with reference to Table 1.

[52358] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1519 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1519 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52359] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1519 gene, herein designated VGAM is inhibition of expression of VGAM1519 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1519 correlate with, and may be deduced from, the identity of the target genes which VGAM1519 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52360] Amyloid Beta Precursor Protein (cytoplasmic tail) Binding Protein 2 (APPBP2, Accession NM\_006380) is a VGAM1519 host target gene. APPBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by APPBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APPBP2 BINDING SITE, designated SEQ ID:13082, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52361] A function of VGAM1519 is therefore inhibition of Amyloid Beta Precursor Protein (cytoplasmic tail) Binding Protein 2 (APPBP2, Accession NM\_006380), a gene which interacts with the basolateral sorting signal of amyloid precursor protein. Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APPBP2. The function of APPBP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM525. Dedicator of Cyto-kinesis 1 (DOCK1, Accession NM\_001380) is another VGAM1519 host target gene. DOCK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DOCK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of DOCK1 BINDING SITE, designated SEQ ID:7051, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52362] Another function of VGAM1519 is therefore inhibition of Dedicator of Cyto-kinesis 1 (DOCK1, Accession NM\_001380), a gene which may function in the extension of cell surfaces. Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DOCK1. The function of DOCK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM564. Fucosyltransferase 5 (alpha (1,3) Fucosyltransferase) (FUT5, Accession NM\_002034) is another VGAM1519 host target gene. FUT5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT5 BINDING SITE, designated SEQ ID:7788, to the nucleotide sequence of

VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52363] Another function of VGAM1519 is therefore inhibition of Fucosyltransferase 5 (alpha (1,3) Fucosyltransferase) (FUT5, Accession NM\_002034), a gene which may catalyse alpha-1,3 glycosidic linkages involved in the expression of vim-2, lewis x/ssea-1 and sialyl lewis x antigens. Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT5. The function of FUT5 has been established by previous studies. Weston et al. (1992) isolated a human alpha-3-fucosyltransferase gene homologous to but distinct from 2 previously reported fucosyltransferase genes: alpha-3,4-fucosyltransferase, thought to represent the human Lewis blood group locus (FUT3; 111100), and an alpha-3-fucosyltransferase expressed in the myeloid lineage (FUT4; 104230). The new enzyme shared 91% amino acid sequence identity with the Lewis blood group fucosyltransferase, yet exhibited only trace amounts of alpha-4-fucosyltransferase activity. By PCR analysis of somatic cell hybrid DNAs, Weston et al. (1992) demonstrated that the gene is located on chromosome 19. They concluded that the gene encodes a 'plasma type'

of alpha-3-fucosyltransferase. McCurley et al. (1995) mapped FUT5 to 19p13.3 by fluorescence in situ hybridization using cosmids containing FUT6 (OMIM Ref. No. 136836) and FUT5. The results indicated that FUT6 lies approximately 70 kb telomeric of FUT5. McCurley et al. (1995) used conventional and pulsed field gel electrophoresis mapping to total genomic DNA and large genomic clones in order to generate a fine map of the cluster of 19p FUT genes. A P1 clone indicated the gene order: cen--FUT5--FUT3--FUT6--tel. FUT5 and FUT3 are separated by 23 kb and FUT3 and FUT6 are separated by 14 kb; these data placed FUT5 and FUT6 closer together than was estimated by fluorescence in situ hybridization. The close proximity and tandem orientation of the 3 genes suggests coordinate regulation. The direction of transcription is toward the telomere in the case of all 3 genes

[52364] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52365] McCurley, R. S.; Recinos, A., III; Olsen, A. S.; Gingrich, J. C.; Szczepaniak, D.; Cameron, H. S.; Krauss, R.; Weston, B. W. : Physical maps of human alpha(1,3)fucosyltransferase genes FUT3-FUT6 on chromosomes 19p13.3 and 11q21.

Genomics 26: 142–146, 1995. ; and

[52366] Weston, B. W.; Nair, R. P.; Larsen, R. D.; Lowe, J. B. : Isolation of a novel human alpha(1,3)fucosyltransferase gene and molecular comparison to the human Lewis blood group alpha(1,3/1.

[52367] Further studies establishing the function and utilities of FUT5 are found in John Hopkins OMIM database record ID 136835, and in cited publications numbered 2177–2179 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Beta 16 (PCDHB16, Accession NM\_020957) is another VGAM1519 host target gene. PCDHB16 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PCDHB16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB16 BINDING SITE, designated SEQ ID:21947, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52368] Another function of VGAM1519 is therefore inhibition of Protocadherin Beta 16 (PCDHB16, Accession NM\_020957), a gene which is a potential calcium-dependent cell–



adhesion protein. Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHB16. The function of PCDHB16 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM931. Peptidylprolyl Isomerase (cyclophilin)-like 1 (PPIL1, Accession NM\_016059) is another VGAM1519 host target gene. PPIL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPIL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPIL1 BINDING SITE, designated SEQ ID:18134, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52369] Another function of VGAM1519 is therefore inhibition of Peptidylprolyl Isomerase (cyclophilin)-like 1 (PPIL1, Accession NM\_016059), a gene which catalyzes the cis-trans isomerization of proline imidic peptide bonds in oligopeptides. Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with PPIL1. The function of PPIL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1135. Ret Proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease) (RET, Accession NM\_020630) is another VGAM1519 host target gene. RET BINDING SITE1 and RET BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RET, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RET BINDING SITE1 and RET BINDING SITE2, designated SEQ ID:21788 and SEQ ID:21962 respectively, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52370] Another function of VGAM1519 is therefore inhibition of Ret Proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease) (RET, Accession NM\_020630), a gene which transduces signals for cell growth and differentiation. Accordingly, utilities of VGAM1519 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with RET. The function of RET and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381.DKFZp762A227 (Accession NM\_014096) is another VGAM1519 host target gene. DKFZp762A227 BINDING SITE1 and DKFZp762A227 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZp762A227, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762A227 BINDING SITE1 and DKFZp762A227 BINDING SITE2, designated SEQ ID:15320 and SEQ ID:19108 respectively, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52371] Another function of VGAM1519 is therefore inhibition of DKFZp762A227 (Accession NM\_014096). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762A227. FLJ14146 (Accession NM\_024709) is another VGAM1519 host target gene. FLJ14146 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14146 BINDING SITE, designated SEQ ID:24031, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52372] Another function of VGAM1519 is therefore inhibition of FLJ14146 (Accession NM\_024709). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14146. FLJ20449 (Accession NM\_017826) is another VGAM1519 host target gene. FLJ20449 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20449 BINDING SITE, designated SEQ ID:19488, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52373] Another function of VGAM1519 is therefore inhibition of

FLJ20449 (Accession NM\_017826). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20449. FLJ23548 (Accession NM\_024590) is another VGAM1519 host target gene. FLJ23548 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23548, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23548 BINDING SITE, designated SEQ ID:23824, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52374] Another function of VGAM1519 is therefore inhibition of FLJ23548 (Accession NM\_024590). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23548. KIAA0016 (Accession NM\_014765) is another VGAM1519 host target gene. KIAA0016 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0016 BINDING SITE, designated SEQ ID:16531, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52375] Another function of VGAM1519 is therefore inhibition of KIAA0016 (Accession NM\_014765). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0016. KIAA1600 (Accession XM\_049351) is another VGAM1519 host target gene. KIAA1600 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1600 BINDING SITE, designated SEQ ID:35394, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52376] Another function of VGAM1519 is therefore inhibition of KIAA1600 (Accession XM\_049351). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1600. MGC11287 (Accession NM\_031464) is another

VGAM1519 host target gene. MGC11287 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11287, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11287 BINDING SITE, designated SEQ ID:25501, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52377] Another function of VGAM1519 is therefore inhibition of MGC11287 (Accession NM\_031464). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11287. MGC17330 (Accession NM\_052880) is another VGAM1519 host target gene. MGC17330 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC17330, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC17330 BINDING SITE, designated SEQ ID:27461, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52378] Another function of VGAM1519 is therefore inhibition of MGC17330 (Accession NM\_052880). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC17330. LOC116068 (Accession XM\_057302) is another VGAM1519 host target gene. LOC116068 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116068, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116068 BINDING SITE, designated SEQ ID:36502, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52379] Another function of VGAM1519 is therefore inhibition of LOC116068 (Accession XM\_057302). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116068. LOC202754 (Accession XM\_095123) is another VGAM1519 host target gene. LOC202754 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202754, corresponding to a HOST TARGET binding site such as BIND-



ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202754 BINDING SITE, designated SEQ ID:40248, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52380] Another function of VGAM1519 is therefore inhibition of LOC202754 (Accession XM\_095123). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202754. LOC90826 (Accession XM\_034321) is another VGAM1519 host target gene. LOC90826 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90826 BINDING SITE, designated SEQ ID:32052, to the nucleotide sequence of VGAM1519 RNA, herein designated VGAM RNA, also designated SEQ ID:4230.

[52381] Another function of VGAM1519 is therefore inhibition of LOC90826 (Accession XM\_034321). Accordingly, utilities of VGAM1519 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90826. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1520 (VGAM1520) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52382] VGAM1520 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1520 was detected is described hereinabove with reference to Figs. 1–8.

[52383] VGAM1520 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus. VGAM1520 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52384] VGAM1520 gene encodes a VGAM1520 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1520 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1520 precursor RNA is designated SEQ ID:1506, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1506 is located at position 74844 relative to the genome of Ectromelia Virus.

- [52385] VGAM1520 precursor RNA folds onto itself, forming VGAM1520 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [52386] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1520 folded precursor RNA into VGAM1520 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1520 RNA is designated SEQ ID:4231, and is provided hereinbelow with reference to the sequence listing part.

[52387] VGAM1520 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1520 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1520 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52388] VGAM1520 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1520 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1520 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1520 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1520 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52389] The complementary binding of VGAM1520 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1520 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1520 host target RNA into VGAM1520 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52390] It is appreciated that VGAM1520 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1520 host target genes. The mRNA of each one of this plurality of VGAM1520 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1520 RNA, herein designated VGAM RNA, and which when bound by VGAM1520 RNA causes

inhibition of translation of respective one or more VGAM1520 host target proteins.

[52391] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1520 gene, herein designated VGAM GENE, on one or more VGAM1520 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52392] It is yet further appreciated that a function of VGAM1520 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1520 include diagnosis, prevention and

treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1520 correlate with, and may be deduced from, the identity of the host target genes which VGAM1520 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52393] Nucleotide sequences of the VGAM1520 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1520 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1520 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1520 are further described hereinbelow with reference to Table 1.

[52394] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1520 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1520 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52395] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1520 gene, herein designated VGAM is inhibition of expression of VGAM1520 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1520 correlate with, and may be deduced from, the identity of the target genes which VGAM1520 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52396] High-mobility Group Box 3 (HMGB3, Accession NM\_005342) is a VGAM1520 host target gene. HMGB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGB3 BINDING SITE, designated SEQ ID:11816, to the nucleotide sequence of VGAM1520 RNA, herein designated VGAM RNA, also designated SEQ ID:4231.

[52397] A function of VGAM1520 is therefore inhibition of High-mobility Group Box 3 (HMGB3, Accession NM\_005342), a gene which plays a fundamental role in DNA replication, nucleosome assembly, and transcription. Accordingly, utilities of VGAM1520 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGB3. The function of HMGB3 and its association with various diseases and clinical conditions, has been es-



established by previous studies, as described hereinabove with reference to VGAM1272.SMAC (Accession NM\_138930) is another VGAM1520 host target gene. SMAC BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SMAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMAC BINDING SITE, designated SEQ ID:29054, to the nucleotide sequence of VGAM1520 RNA, herein designated VGAM RNA, also designated SEQ ID:4231.

[52398] Another function of VGAM1520 is therefore inhibition of SMAC (Accession NM\_138930), a gene which promotes apoptosis via caspase activation. Accordingly, utilities of VGAM1520 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMAC. The function of SMAC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.DKFZp547D155 (Accession XM\_046977) is another VGAM1520 host target gene. DKFZp547D155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DK-

FZp547D155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547D155 BINDING SITE, designated SEQ ID:34865, to the nucleotide sequence of VGAM1520 RNA, herein designated VGAM RNA, also designated SEQ ID:4231.

[52399] Another function of VGAM1520 is therefore inhibition of DKFZp547D155 (Accession XM\_046977). Accordingly, utilities of VGAM1520 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547D155. FLJ11126 (Accession NM\_018332) is another VGAM1520 host target gene. FLJ11126 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11126, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11126 BINDING SITE, designated SEQ ID:20333, to the nucleotide sequence of VGAM1520 RNA, herein designated VGAM RNA, also designated SEQ ID:4231.

[52400] Another function of VGAM1520 is therefore inhibition of FLJ11126 (Accession NM\_018332). Accordingly, utilities of

VGAM1520 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11126. FLJ12704 (Accession NM\_024998) is another VGAM1520 host target gene. FLJ12704 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12704 BINDING SITE, designated SEQ ID:24560, to the nucleotide sequence of VGAM1520 RNA, herein designated VGAM RNA, also designated SEQ ID:4231.

[52401] Another function of VGAM1520 is therefore inhibition of FLJ12704 (Accession NM\_024998). Accordingly, utilities of VGAM1520 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12704. FLJ20309 (Accession NM\_017759) is another VGAM1520 host target gene. FLJ20309 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20309, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20309

BINDING SITE, designated SEQ ID:19370, to the nucleotide sequence of VGAM1520 RNA, herein designated VGAM RNA, also designated SEQ ID:4231.

[52402] Another function of VGAM1520 is therefore inhibition of FLJ20309 (Accession NM\_017759). Accordingly, utilities of VGAM1520 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20309. LOC148696 (Accession XM\_097505) is another VGAM1520 host target gene. LOC148696 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148696 BINDING SITE, designated SEQ ID:40892, to the nucleotide sequence of VGAM1520 RNA, herein designated VGAM RNA, also designated SEQ ID:4231.

[52403] Another function of VGAM1520 is therefore inhibition of LOC148696 (Accession XM\_097505). Accordingly, utilities of VGAM1520 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148696. LOC149276 (Accession XM\_097621) is another VGAM1520 host target gene. LOC149276 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149276 BINDING SITE, designated SEQ ID:40973, to the nucleotide sequence of VGAM1520 RNA, herein designated VGAM RNA, also designated SEQ ID:4231.

[52404] Another function of VGAM1520 is therefore inhibition of LOC149276 (Accession XM\_097621). Accordingly, utilities of VGAM1520 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149276. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1521 (VGAM1521) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52405] VGAM1521 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1521 was detected is described hereinabove with reference to Figs. 1-8.

[52406] VGAM1521 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus.

VGAM1521 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52407] VGAM1521 gene encodes a VGAM1521 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1521 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1521 precursor RNA is designated SEQ ID:1507, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1507 is located at position 67798 relative to the genome of Ectromelia Virus.

[52408] VGAM1521 precursor RNA folds onto itself, forming VGAM1521 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[52409] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1521 folded precursor RNA into VGAM1521 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1521 RNA is designated SEQ ID:4232, and is provided hereinbelow with reference to the sequence listing part.

[52410] VGAM1521 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1521 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1521 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52411] VGAM1521 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1521 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1521 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1521 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1521 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52412] The complementary binding of VGAM1521 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1521 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE



II and BINDING SITE III, inhibits translation of VGAM1521 host target RNA into VGAM1521 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52413] It is appreciated that VGAM1521 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1521 host target genes. The mRNA of each one of this plurality of VGAM1521 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1521 RNA, herein designated VGAM RNA, and which when bound by VGAM1521 RNA causes inhibition of translation of respective one or more VGAM1521 host target proteins.

[52414] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1521 gene, herein designated VGAM GENE, on one or more VGAM1521 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52415] It is yet further appreciated that a function of VGAM1521 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1521 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1521 correlate with, and may be deduced from, the identity of the host target genes which VGAM1521 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52416] Nucleotide sequences of the VGAM1521 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1521 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1521 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1521 are further described hereinbelow with reference to Table 1.

[52417] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1521 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1521 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52418] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1521 gene, herein designated VGAM is inhibition of expression of VGAM1521 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1521 correlate with, and may be deduced from, the identity of the target genes which VGAM1521 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52419] TRIM (Accession NM\_016388) is a VGAM1521 host target gene. TRIM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of TRIM BINDING SITE, designated SEQ ID:18528, to the nucleotide sequence of VGAM1521 RNA, herein designated VGAM RNA, also designated SEQ ID:4232.

[52420] A function of VGAM1521 is therefore inhibition of TRIM (Accession NM\_016388), a gene which plays a role in recruiting signaling proteins to the plasma membrane upon T-cell receptor (TCR) complex activation in T cells. Accordingly, utilities of VGAM1521 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM. The function of TRIM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM227.PRO2037 (Accession NM\_018616) is another VGAM1521 host target gene. PRO2037 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO2037, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2037 BINDING SITE, designated SEQ ID:20687, to the nucleotide sequence of VGAM1521 RNA, herein designated VGAM RNA, also designated SEQ ID:4232.

[52421] Another function of VGAM1521 is therefore inhibition of PRO2037 (Accession NM\_018616). Accordingly, utilities of VGAM1521 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2037. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1522 (VGAM1522) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52422] VGAM1522 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1522 was detected is described hereinabove with reference to Figs. 1-8.

[52423] VGAM1522 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus. VGAM1522 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52424] VGAM1522 gene encodes a VGAM1522 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1522 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1522 precursor RNA is designated SEQ ID:1508, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1508 is located at position 72179 relative to the genome of Ectromelia Virus.

- [52425] VGAM1522 precursor RNA folds onto itself, forming VGAM1522 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [52426] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1522 folded precursor RNA into VGAM1522 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1522 RNA is designated SEQ ID:4233, and is provided hereinbelow with reference to the sequence listing part.

[52427] VGAM1522 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1522 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1522 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[52428] VGAM1522 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1522 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1522 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1522 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1522 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52429] The complementary binding of VGAM1522 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1522 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1522 host target RNA into VGAM1522 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52430] It is appreciated that VGAM1522 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1522 host target genes. The mRNA of each one of this plurality of VGAM1522 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1522 RNA, herein designated VGAM RNA, and which when bound by VGAM1522 RNA causes inhibition of translation of respective one or more VGAM1522 host target proteins.

[52431] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1522 gene, herein designated VGAM GENE, on one or more VGAM1522 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52432] It is yet further appreciated that a function of VGAM1522 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1522 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1522 correlate with, and may be deduced from, the identity of the host target genes which VGAM1522 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52433] Nucleotide sequences of the VGAM1522 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1522 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1522 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1522 are further described hereinbelow with reference to Table 1.

[52434] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1522 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1522 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[52435] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1522 gene, herein designated VGAM is inhibition of expression of VGAM1522 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1522 correlate with, and may be deduced from, the identity of the target genes which VGAM1522 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52436] KIAA1691 (Accession XM\_166523) is a VGAM1522 host target gene. KIAA1691 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1691, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1691 BINDING SITE, designated SEQ ID:44464, to the nucleotide sequence of VGAM1522 RNA, herein designated VGAM RNA, also designated SEQ ID:4233.

[52437] A function of VGAM1522 is therefore inhibition of KIAA1691 (Accession XM\_166523). Accordingly, utilities of VGAM1522 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1691. LOC154813 (Accession XM\_088051) is another VGAM1522 host target gene. LOC154813 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154813 BINDING SITE, designated SEQ ID:39492, to the nucleotide sequence of VGAM1522 RNA, herein designated VGAM RNA, also designated SEQ ID:4233.

[52438] Another function of VGAM1522 is therefore inhibition of LOC154813 (Accession XM\_088051). Accordingly, utilities of VGAM1522 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154813. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1523 (VGAM1523) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52439] VGAM1523 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1523 was detected is described hereinabove with reference to Figs. 1–8.

[52440] VGAM1523 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus.

VGAM1523 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52441] VGAM1523 gene encodes a VGAM1523 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1523 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1523 precursor RNA is designated SEQ ID:1509, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1509 is located at position 79940 relative to the genome of Cowpox Virus.

[52442] VGAM1523 precursor RNA folds onto itself, forming VGAM1523 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52443] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1523 folded precursor RNA into VGAM1523 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1523 RNA is designated SEQ ID:4234, and is provided hereinbelow with reference to the sequence listing part.

[52444] VGAM1523 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1523 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1523 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52445] VGAM1523 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1523 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1523 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1523 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1523 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[52446] The complementary binding of VGAM1523 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1523 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1523 host target RNA into VGAM1523 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52447] It is appreciated that VGAM1523 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1523 host target genes. The mRNA of each one of this plurality of VGAM1523 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1523 RNA, herein designated VGAM RNA, and which when bound by VGAM1523 RNA causes inhibition of translation of respective one or more VGAM1523 host target proteins.

[52448] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1523 gene, herein designated VGAM GENE, on one or more VGAM1523 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52449] It is yet further appreciated that a function of VGAM1523 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1523 correlate with, and may be deduced from, the identity of the host target genes which VGAM1523 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52450] Nucleotide sequences of the VGAM1523 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1523 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1523 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1523 are further described hereinbelow with reference to Table 1.

[52451] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1523 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1523 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52452] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1523 gene, herein designated VGAM is inhibition of expression of VGAM1523 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1523 correlate with, and may be deduced from, the identity of the target genes which VGAM1523 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52453] ATP-binding Cassette, Sub-family B (MDR/TAP), Member 10 (ABCB10, Accession NM\_012089) is a VGAM1523 host target gene. ABCB10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA en-

coded by ABCB10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCB10 BINDING SITE, designated SEQ ID:14374, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52454] A function of VGAM1523 is therefore inhibition of ATP-binding Cassette, Sub-family B (MDR/TAP), Member 10 (ABCB10, Accession NM\_012089), a gene which a member of the superfamily of ATP-binding cassette (ABC) transporters. Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCB10. The function of ABCB10 has been established by previous studies. For background information on the ATP-binding cassette (ABC) family of transporter proteins, see ABCA4 (OMIM Ref. No. 601691). In addition to the 'full' ABC transporters with 2 transmembrane domains and 2 nucleotide-binding domains, there are 'half' proteins that contain only 1 of each domain (e.g., ABCB1; 171050). Allikmets et al. (1995) mapped a partial EST corresponding to the ABCB10 gene to 1q42. However, using FISH, Zhang et al. (2000)

mapped the full-length ABCB10 gene to 15q13–q14. PCR and Southern blot analysis of genomic DNA showed that the chromosome 15 localization represents a pseudogene.

[52455] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52456] Allikmets, R.; Gerrard, B.; Glavac, D.; Ravnik–Glavac, M.; Jenkins, N. A.; Gilbert, D. J.; Copeland, N. G.; Modi, W.; Dean, M. : Characterization and mapping of three new mammalian ATP–binding transporter genes from an EST database. *Mammalian Genome* 6: 114–117, 1995. ; and

[52457] Zhang, F.; Hogue, D. L.; Liu, L.; Fisher, C. L.; Hui, D.; Childs, S.; Ling, V. : M–ABC2, a new human mitochondrial ATP–binding cassette membrane protein. *FEBS Lett.* 478: 89–94, 2000.

[52458] Further studies establishing the function and utilities of ABCB10 are found in John Hopkins OMIM database record ID 605454, and in cited publications numbered 963–964 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Adducin 1 (alpha) (ADD1, Accession NM\_014189) is another VGAM1523 host target gene. ADD1 BINDING SITE1 and ADD1 BINDING SITE2 are HOST TARGET binding sites found in untrans–

lated regions of mRNA encoded by ADD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADD1 BINDING SITE1 and ADD1 BINDING SITE2, designated SEQ ID:15470 and SEQ ID:15474 respectively, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52459] Another function of VGAM1523 is therefore inhibition of Adducin 1 (alpha) (ADD1, Accession NM\_014189), a gene which membrane-cytoskeleton- protein that promotes the assembly of the spectrin-actin network. Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADD1. The function of ADD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM474. Chemokine (C-C motif) Receptor 9 (CCR9, Accession NM\_006641) is another VGAM1523 host target gene. CCR9 BINDING SITE1 and CCR9 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCR9, corresponding to HOST TARGET binding sites such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR9 BINDING SITE1 and CCR9 BINDING SITE2, designated SEQ ID:13432 and SEQ ID:22412 respectively, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52460] Another function of VGAM1523 is therefore inhibition of Chemokine (C-C motif) Receptor 9 (CCR9, Accession NM\_006641), a gene which binds beta-chemokine family and subsequently transduces a signal by increasing the intracellular calcium ions level. Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR9. The function of CCR9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1324.CGTHBA (Accession NM\_012075) is another VGAM1523 host target gene. CGTHBA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGTHBA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGTHBA

BINDING SITE, designated SEQ ID:14364, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52461] Another function of VGAM1523 is therefore inhibition of CGTHBA (Accession NM\_012075). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGTHBA. Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM\_114147) is another VGAM1523 host target gene. EIF1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF1A BINDING SITE, designated SEQ ID:42721, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52462] Another function of VGAM1523 is therefore inhibition of Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM\_114147), a gene which seems to be required for maximal rate of protein biosynthesis. Accordingly, utilities of VGAM1523 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with EIF1A. The function of EIF1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440) is another VGAM1523 host target gene. EXTL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EXTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL3 BINDING SITE, designated SEQ ID:7171, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52463] Another function of VGAM1523 is therefore inhibition of Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440), a gene which is a member of the multiple exostoses gene family. Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL3. The function of EXTL3 and its association with various diseases and clinical conditions, has been established by previous



studies, as described hereinabove with reference to VGAM95. Growth Hormone Receptor (GHR, Accession NM\_000163) is another VGAM1523 host target gene. GHR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GHR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GHR BINDING SITE, designated SEQ ID:5671, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52464] Another function of VGAM1523 is therefore inhibition of Growth Hormone Receptor (GHR, Accession NM\_000163). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GHR. Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262) is another VGAM1523 host target gene. HS2ST1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HS2ST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

HS2ST1 BINDING SITE, designated SEQ ID:14576, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52465] Another function of VGAM1523 is therefore inhibition of Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS2ST1. Nucleobindin 1 (NUCB1, Accession NM\_006184) is another VGAM1523 host target gene. NUCB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUCB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUCB1 BINDING SITE, designated SEQ ID:12851, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52466] Another function of VGAM1523 is therefore inhibition of Nucleobindin 1 (NUCB1, Accession NM\_006184), a gene which may have a role in calcium homeostasis. Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with NUCB1. The function of NUCB1 has been established by previous studies. Lupus-prone mice with the lymphoproliferation (lpr) mutation produced large amounts of antibody against both single-stranded and double-stranded DNA (Theofilopoulos and Dixon, 1985). The primary defect is a deficiency in expression of the Fas gene (OMIM Ref. No. 134637). Nucleobindin (Nuc) was first identified as a secreted protein of 55 kD that promotes production of DNA-specific antibodies in these mice (Kanai et al., 1993). Analysis of cDNA that encodes mouse Nuc demonstrated that the protein is composed of a signal peptide, a DNA-binding site, 2 calcium-binding motifs, and a leucine zipper (Miura et al., 1992). Miura et al. (1996) analyzed the organization of the human NUC gene. It consists of 13 exons that are distributed in a region of 32 kb. The gene encodes a 461-amino acid polypeptide. The functional motifs identified in the murine protein are encoded in corresponding human exons. A 2.4-kb NUC transcript was expressed in all organs examined. Comparison of nucleotide sequences in the promoter regions between human and mouse NUC genes revealed several conserved sequences. The promoter is of the TATA-less type, and transcription starts at multiple

sites in both the human and the mouse genes. These features suggested to them that NUC may play a role as a housekeeping gene. By PCR analysis of human/hamster somatic cell hybrids and by fluorescence in situ hybridization, Miura et al. (1996) mapped the NUC gene to 19q13.2–q13.4.

[52467] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52468] Kanai, Y.; Miura, K.; Uehara, T.; Amagai, M.; Takeda, O.; Tanuma, S.; Kurosawa, Y. : Natural occurrence of Nuc in the sera of autoimmune–prone MRL/lpr mice. *Biochem. Biophys. Res. Commun.* 196: 729–736, 1993. ; and

[52469] Miura, K.; Hirai, M.; Kanai, Y.; Kurosawa, Y. : Organization of the human gene for nucleobindin (NUC) and its chromosomal assignment to 19q13.2–q13.4. *Genomics* 34: 181–186, 1996.

[52470] Further studies establishing the function and utilities of NUCB1 are found in John Hopkins OMIM database record ID 601323, and in cited publications numbered 9385–938 and 10961 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CDC42 Binding Protein Kinase Beta (DMPK–like) (CDC42BPB, Ac–

cession NM\_006035) is another VGAM1523 host target gene. CDC42BPB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC42BPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC42BPB BINDING SITE, designated SEQ ID:12658, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52471] Another function of VGAM1523 is therefore inhibition of CDC42 Binding Protein Kinase Beta (DMPK-like) (CDC42BPB, Accession NM\_006035). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC42BPB. DKFZP566B183 (Accession NM\_015509) is another VGAM1523 host target gene. DKFZP566B183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566B183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566B183 BINDING SITE, designated SEQ

ID:17769, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52472] Another function of VGAM1523 is therefore inhibition of DKFZP566B183 (Accession NM\_015509). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566B183. DKFZP566I1024 (Accession XM\_046506) is another VGAM1523 host target gene. DKFZP566I1024 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566I1024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566I1024 BINDING SITE, designated SEQ ID:34735, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52473] Another function of VGAM1523 is therefore inhibition of DKFZP566I1024 (Accession XM\_046506). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566I1024. DKFZp761B0514 (Accession

NM\_032289) is another VGAM1523 host target gene. DKFZp761B0514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761B0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761B0514 BINDING SITE, designated SEQ ID:26053, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52474] Another function of VGAM1523 is therefore inhibition of DKFZp761B0514 (Accession NM\_032289). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761B0514. FLJ13305 (Accession XM\_117270) is another VGAM1523 host target gene. FLJ13305 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13305 BINDING SITE, designated SEQ ID:43345, to the nucleotide sequence of VGAM1523 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4234.

[52475] Another function of VGAM1523 is therefore inhibition of FLJ13305 (Accession XM\_117270). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13305. KIAA0265 (Accession XM\_045954) is another VGAM1523 host target gene. KIAA0265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0265 BINDING SITE, designated SEQ ID:34620, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52476] Another function of VGAM1523 is therefore inhibition of KIAA0265 (Accession XM\_045954). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0265. KIAA1117 (Accession XM\_028219) is another VGAM1523 host target gene. KIAA1117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1117, corresponding to



a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1117 BINDING SITE, designated SEQ ID:30632, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52477] Another function of VGAM1523 is therefore inhibition of KIAA1117 (Accession XM\_028219). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1117. KIAA1319 (Accession NM\_020770) is another VGAM1523 host target gene. KIAA1319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1319 BINDING SITE, designated SEQ ID:21870, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52478] Another function of VGAM1523 is therefore inhibition of KIAA1319 (Accession NM\_020770). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1319. Nudix (nucleoside diphosphate linked moiety X)-type Motif 13 (NUDT13, Accession XM\_032512) is another VGAM1523 host target gene. NUDT13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUDT13 BINDING SITE, designated SEQ ID:31664, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52479] Another function of VGAM1523 is therefore inhibition of Nudix (nucleoside diphosphate linked moiety X)-type Motif 13 (NUDT13, Accession XM\_032512). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUDT13. SSH2 (Accession XM\_030846) is another VGAM1523 host target gene. SSH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of SSH2 BINDING SITE, designated SEQ ID:31176, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52480] Another function of VGAM1523 is therefore inhibition of SSH2 (Accession XM\_030846). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH2. Signal Sequence Receptor, Alpha (translocon-associated protein alpha) (SSR1, Accession NM\_003144) is another VGAM1523 host target gene. SSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSR1 BINDING SITE, designated SEQ ID:9113, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52481] Another function of VGAM1523 is therefore inhibition of Signal Sequence Receptor, Alpha (translocon-associated protein alpha) (SSR1, Accession NM\_003144). Accordingly, utilities of VGAM1523 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with SSR1. TAF9-like RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 31kDa (TAF9L, Accession NM\_015975) is another VGAM1523 host target gene. TAF9L BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TAF9L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF9L BINDING SITE, designated SEQ ID:18072, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52482] Another function of VGAM1523 is therefore inhibition of TAF9-like RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 31kDa (TAF9L, Accession NM\_015975). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF9L. LOC115294 (Accession XM\_054302) is another VGAM1523 host target gene. LOC115294 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC115294, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115294 BINDING SITE, designated SEQ ID:36145, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52483] Another function of VGAM1523 is therefore inhibition of LOC115294 (Accession XM\_054302). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115294. LOC150271 (Accession XM\_097859) is another VGAM1523 host target gene. LOC150271 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41166, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52484] Another function of VGAM1523 is therefore inhibition of LOC150271 (Accession XM\_097859). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC150271. LOC151877 (Accession XM\_098132) is another VGAM1523 host target gene. LOC151877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151877 BINDING SITE, designated SEQ ID:41398, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52485] Another function of VGAM1523 is therefore inhibition of LOC151877 (Accession XM\_098132). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151877. LOC152300 (Accession XM\_087432) is another VGAM1523 host target gene. LOC152300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152300 BINDING SITE, designated SEQ ID:39248, to

the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52486] Another function of VGAM1523 is therefore inhibition of LOC152300 (Accession XM\_087432). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152300. LOC154084 (Accession XM\_098468) is another VGAM1523 host target gene. LOC154084 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154084 BINDING SITE, designated SEQ ID:41685, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52487] Another function of VGAM1523 is therefore inhibition of LOC154084 (Accession XM\_098468). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154084. LOC158402 (Accession XM\_098936) is another VGAM1523 host target gene. LOC158402 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC158402, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158402 BINDING SITE, designated SEQ ID:41976, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52488] Another function of VGAM1523 is therefore inhibition of LOC158402 (Accession XM\_098936). Accordingly, utilities of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158402. LOC162333 (Accession XM\_102591) is another VGAM1523 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42124, to the nucleotide sequence of VGAM1523 RNA, herein designated VGAM RNA, also designated SEQ ID:4234.

[52489] Another function of VGAM1523 is therefore inhibition of LOC162333 (Accession XM\_102591). Accordingly, utilities



of VGAM1523 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1524 (VGAM1524) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52490] VGAM1524 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1524 was detected is described hereinabove with reference to Figs. 1-8.

[52491] VGAM1524 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1524 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52492] VGAM1524 gene encodes a VGAM1524 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1524 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1524 precursor RNA is designated SEQ ID:1510, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1510 is located at position 76982 relative to the genome of Cowpox Virus.

- [52493] VGAM1524 precursor RNA folds onto itself, forming VGAM1524 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [52494] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1524 folded precursor RNA into VGAM1524 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1524 RNA is designated SEQ ID:4235, and

is provided hereinbelow with reference to the sequence listing part.

[52495] VGAM1524 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1524 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1524 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[52496] VGAM1524 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1524 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1524 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1524 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1524 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52497] The complementary binding of VGAM1524 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1524 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1524 host target RNA into VGAM1524 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52498] It is appreciated that VGAM1524 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1524 host target genes. The mRNA of each one of this plurality of VGAM1524 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1524 RNA, herein designated VGAM RNA, and which when bound by VGAM1524 RNA causes inhibition of translation of respective one or more VGAM1524 host target proteins.

[52499] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1524 gene, herein designated VGAM GENE, on one or more VGAM1524 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52500] It is yet further appreciated that a function of VGAM1524 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1524 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1524 correlate with, and may be deduced from, the identity of the host target genes which VGAM1524 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52501] Nucleotide sequences of the VGAM1524 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1524 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1524 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1524 are further described hereinbelow with reference to Table 1.

[52502] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1524 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1524 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52503] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1524 gene, herein designated VGAM is inhibition of expression of VGAM1524 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1524 correlate with, and may be deduced from, the identity of the target genes which VGAM1524 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52504] Transmembrane, Cochlear Expressed, 1 (TMC1, Accession NM\_138691) is a VGAM1524 host target gene. TMC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TMC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMC1 BINDING SITE, designated SEQ ID:28931, to the nucleotide sequence of VGAM1524 RNA, herein designated VGAM RNA, also designated SEQ ID:4235.

[52505] A function of VGAM1524 is therefore inhibition of Transmembrane, Cochlear Expressed, 1 (TMC1, Accession NM\_138691), a gene which is required for normal function of cochlear hair cells. Accordingly, utilities of VGAM1524 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMC1. The func-

tion of TMC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM554.KIAA0546 (Accession XM\_049055) is another VGAM1524 host target gene. KIAA0546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0546 BINDING SITE, designated SEQ ID:35332, to the nucleotide sequence of VGAM1524 RNA, herein designated VGAM RNA, also designated SEQ ID:4235.

[52506] Another function of VGAM1524 is therefore inhibition of KIAA0546 (Accession XM\_049055). Accordingly, utilities of VGAM1524 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0546. LOC143879 (Accession XM\_084666) is another VGAM1524 host target gene. LOC143879 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143879, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the



complementarity of the nucleotide sequences of LOC143879 BINDING SITE, designated SEQ ID:37656, to the nucleotide sequence of VGAM1524 RNA, herein designated VGAM RNA, also designated SEQ ID:4235.

[52507] Another function of VGAM1524 is therefore inhibition of LOC143879 (Accession XM\_084666). Accordingly, utilities of VGAM1524 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143879. LOC153222 (Accession XM\_087631) is another VGAM1524 host target gene. LOC153222 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153222 BINDING SITE, designated SEQ ID:39366, to the nucleotide sequence of VGAM1524 RNA, herein designated VGAM RNA, also designated SEQ ID:4235.

[52508] Another function of VGAM1524 is therefore inhibition of LOC153222 (Accession XM\_087631). Accordingly, utilities of VGAM1524 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153222. LOC219988 (Accession XM\_166223) is an-

other VGAM1524 host target gene. LOC219988 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219988 BINDING SITE, designated SEQ ID:44041, to the nucleotide sequence of VGAM1524 RNA, herein designated VGAM RNA, also designated SEQ ID:4235.

[52509] Another function of VGAM1524 is therefore inhibition of LOC219988 (Accession XM\_166223). Accordingly, utilities of VGAM1524 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219988. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1525 (VGAM1525) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52510] VGAM1525 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1525 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[52511] VGAM1525 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus.

VGAM1525 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52512] VGAM1525 gene encodes a VGAM1525 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1525 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1525 precursor RNA is designated SEQ ID:1511, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1511 is located at position 62387 relative to the genome of Camelpox Virus.

[52513] VGAM1525 precursor RNA folds onto itself, forming VGAM1525 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52514] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1525 folded precursor RNA into VGAM1525 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1525 RNA is designated SEQ ID:4236, and is provided hereinbelow with reference to the sequence listing part.

[52515] VGAM1525 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1525 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1525 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52516] VGAM1525 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1525 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1525 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1525 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1525 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52517] The complementary binding of VGAM1525 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1525 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1525 host target RNA into VGAM1525 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52518] It is appreciated that VGAM1525 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1525 host target genes. The mRNA of each one of this plurality of VGAM1525 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1525 RNA, herein designated VGAM RNA, and which when bound by VGAM1525 RNA causes inhibition of translation of respective one or more VGAM1525 host target proteins.

[52519] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1525 gene, herein designated VGAM GENE, on one or more VGAM1525 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52520] It is yet further appreciated that a function of VGAM1525 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1525 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1525 correlate with, and may be deduced from, the identity of the host target genes which VGAM1525 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52521] Nucleotide sequences of the VGAM1525 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1525 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1525 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1525 are further described hereinbelow with reference to Table 1.

[52522] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1525 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1525 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52523] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1525 gene, herein designated VGAM is inhibition of expression of VGAM1525 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1525 correlate with, and may be deduced from, the identity of the target genes which VGAM1525 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52524] LOC170409 (Accession XM\_096330) is a VGAM1525 host target gene. LOC170409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or



BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170409 BINDING SITE, designated SEQ ID:40314, to the nucleotide sequence of VGAM1525 RNA, herein designated VGAM RNA, also designated SEQ ID:4236.

[52525] A function of VGAM1525 is therefore inhibition of LOC170409 (Accession XM\_096330). Accordingly, utilities of VGAM1525 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170409. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1526 (VGAM1526) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52526] VGAM1526 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1526 was detected is described hereinabove with reference to Figs. 1-8.

[52527] VGAM1526 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus. VGAM1526 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[52528] VGAM1526 gene encodes a VGAM1526 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1526 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1526 precursor RNA is designated SEQ ID:1512, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1512 is located at position 71872 relative to the genome of Ectromelia Virus.

[52529] VGAM1526 precursor RNA folds onto itself, forming VGAM1526 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52530] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1526 folded precursor RNA into VGAM1526

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1526 RNA is designated SEQ ID:4237, and is provided hereinbelow with reference to the sequence listing part.

[52531] VGAM1526 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1526 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1526 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52532] VGAM1526 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1526 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1526 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1526 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1526 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52533] The complementary binding of VGAM1526 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1526 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1526 host target RNA into VGAM1526 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[52534] It is appreciated that VGAM1526 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1526 host target genes. The mRNA of each one of this plurality of VGAM1526 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1526 RNA, herein designated VGAM RNA, and which when bound by VGAM1526 RNA causes inhibition of translation of respective one or more VGAM1526 host target proteins.

[52535] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1526 gene, herein designated VGAM GENE, on one or more VGAM1526 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52536] It is yet further appreciated that a function of VGAM1526 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1526 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1526 correlate with, and may be deduced from, the identity of the host target genes which VGAM1526 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52537] Nucleotide sequences of the VGAM1526 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1526 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1526 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1526 are further described hereinbelow with reference to Table 1.

[52538] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1526 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1526 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52539] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1526 gene, herein designated VGAM is inhibition of expression of VGAM1526 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1526 correlate with, and may be deduced from, the identity of the target genes which VGAM1526 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52540] Ets Variant Gene 5 (ets-related molecule) (ETV5, Accession NM\_004454) is a VGAM1526 host target gene. ETV5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ETV5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ETV5 BINDING SITE, designated SEQ ID:10749, to the nucleotide sequence of VGAM1526 RNA, herein designated

VGAM RNA, also designated SEQ ID:4237.

[52541] A function of VGAM1526 is therefore inhibition of Ets Variant Gene 5 (ets-related molecule) (ETV5, Accession NM\_004454), a gene which DNA binding protein of the Ets oncoprotein family. Accordingly, utilities of VGAM1526 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ETV5. The function of ETV5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1171.WW Domain Containing Oxidoreductase (WWOX, Accession NM\_016373) is another VGAM1526 host target gene. WWOX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WWOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WWOX BINDING SITE, designated SEQ ID:18507, to the nucleotide sequence of VGAM1526 RNA, herein designated VGAM RNA, also designated SEQ ID:4237.

[52542] Another function of VGAM1526 is therefore inhibition of WW Domain Containing Oxidoreductase (WWOX, Acces-



sion NM\_016373), a gene which involves in protein-protein interactions and may contribute to the biologic consequences of DNA instability. Accordingly, utilities of VGAM1526 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WWOX. The function of WWOX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM644. Cab45 (Accession NM\_016547) is another VGAM1526 host target gene. Cab45 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Cab45, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Cab45 BINDING SITE, designated SEQ ID:18620, to the nucleotide sequence of VGAM1526 RNA, herein designated VGAM RNA, also designated SEQ ID:4237.

[52543] Another function of VGAM1526 is therefore inhibition of Cab45 (Accession NM\_016547). Accordingly, utilities of VGAM1526 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Cab45. Fig. 1 further provides a conceptual description of a novel

bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1527 (VGAM1527) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52544] VGAM1527 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1527 was detected is described hereinabove with reference to Figs. 1–8.

[52545] VGAM1527 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1527 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52546] VGAM1527 gene encodes a VGAM1527 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1527 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1527 precursor RNA is designated SEQ ID:1513, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1513 is located at position 68087 relative to the

genome of Camelpox Virus.

[52547] VGAM1527 precursor RNA folds onto itself, forming VGAM1527 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52548] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1527 folded precursor RNA into VGAM1527 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 88%) nucleotide sequence of VGAM1527 RNA is designated SEQ ID:4238, and is provided hereinbelow with reference to the sequence listing part.

[52549] VGAM1527 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1527 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1527 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[52550] VGAM1527 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1527 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1527 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1527 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1527 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[52551] The complementary binding of VGAM1527 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1527 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1527 host target RNA into VGAM1527 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52552] It is appreciated that VGAM1527 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1527 host target genes. The mRNA of each one of this plurality of VGAM1527 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1527 RNA, herein designated VGAM RNA, and which when bound by VGAM1527 RNA causes inhibition of translation of respective one or more VGAM1527 host target proteins.

[52553] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1527 gene, herein designated VGAM GENE, on one or more VGAM1527 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52554] It is yet further appreciated that a function of VGAM1527 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1527 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1527 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1527 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52555] Nucleotide sequences of the VGAM1527 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1527 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1527 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1527 are further described hereinbelow with reference to Table 1.

[52556] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1527 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1527 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52557] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1527 gene, herein designated VGAM is inhibition of expression of VGAM1527 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1527 correlate with, and may be deduced

from, the identity of the target genes which VGAM1527 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52558] Ankyrin 3, Node of Ranvier (ankyrin G) (ANK3, Accession NM\_020987) is a VGAM1527 host target gene. ANK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK3 BINDING SITE, designated SEQ ID:21980, to the nucleotide sequence of VGAM1527 RNA, herein designated VGAM RNA, also designated SEQ ID:4238.

[52559] A function of VGAM1527 is therefore inhibition of Ankyrin 3, Node of Ranvier (ankyrin G) (ANK3, Accession NM\_020987), a gene which plays key roles in activities such as cell motility, activation, proliferation. Accordingly, utilities of VGAM1527 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK3. The function of ANK3 has been established by previous studies. Tse et al. (1991) studied immunoreactive isoforms of erythrocyte ankyrin found in nonerythroid tissues. Using an erythrocyte ankyrin cDNA clone as a hy-



bridization probe, they isolated a clone from a human genomic library that hybridized at low but not at high stringency. Further studies suggested that the clone represented part of a gene for nonerythroid ankyrin, which they designated ANK2. By analysis of somatic cell hybrids and by fluorescence in situ hybridization, they assigned ANK2 to 4q25–q27. Otto et al. (1991) isolated and sequenced cDNAs related to 2 brain ankyrin isoforms and showed that they are produced through alternative splicing of the mRNA from a single gene. By analysis of human/rodent cell hybrids, Otto et al. (1991) assigned the brain ankyrin gene to chromosome 4.

[52560] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52561] Otto, E.; Kunimoto, M.; McLaughlin, T.; Bennett, V. : Isolation and characterization of cDNAs encoding human brain ankyrins reveal a family of alternatively spliced genes. *J. Cell Biol.* 114: 241–253, 1991. ; and

[52562] Tse, W. T.; Menninger, J. C.; Yang–Feng, T. L.; Francke, U.; Sahr, K. E.; Lux, S. E.; Ward, D. C.; Forget, B. G. : Isolation and chromosomal localization of a novel non–erythroid ankyri.

[52563] Further studies establishing the function and utilities of ANK3 are found in John Hopkins OMIM database record ID 600465, and in cited publications numbered 1607, 672 and 7731 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ22029 (Accession NM\_024949) is another VGAM1527 host target gene. FLJ22029 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22029, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22029 BINDING SITE, designated SEQ ID:24503, to the nucleotide sequence of VGAM1527 RNA, herein designated VGAM RNA, also designated SEQ ID:4238.

[52564] Another function of VGAM1527 is therefore inhibition of FLJ22029 (Accession NM\_024949). Accordingly, utilities of VGAM1527 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22029. KIAA1579 (Accession NM\_018211) is another VGAM1527 host target gene. KIAA1579 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1579, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1579 BINDING SITE, designated SEQ ID:20115, to the nucleotide sequence of VGAM1527 RNA, herein designated VGAM RNA, also designated SEQ ID:4238.

[52565] Another function of VGAM1527 is therefore inhibition of KIAA1579 (Accession NM\_018211). Accordingly, utilities of VGAM1527 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1579. LOC149153 (Accession XM\_097599) is another VGAM1527 host target gene. LOC149153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149153 BINDING SITE, designated SEQ ID:40961, to the nucleotide sequence of VGAM1527 RNA, herein designated VGAM RNA, also designated SEQ ID:4238.

[52566] Another function of VGAM1527 is therefore inhibition of LOC149153 (Accession XM\_097599). Accordingly, utilities of VGAM1527 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC149153. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1528 (VGAM1528) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52567] VGAM1528 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1528 was detected is described hereinabove with reference to Figs. 1–8.

[52568] VGAM1528 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus. VGAM1528 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52569] VGAM1528 gene encodes a VGAM1528 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1528 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1528 precursor RNA is desig-

nated SEQ ID:1514, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1514 is located at position 72786 relative to the genome of Ectromelia Virus.

- [52570] VGAM1528 precursor RNA folds onto itself, forming VGAM1528 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [52571] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1528 folded precursor RNA into VGAM1528 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1528 RNA is designated SEQ ID:4239, and is provided hereinbelow with reference to the sequence

listing part.

[52572] VGAM1528 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1528 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1528 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52573] VGAM1528 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1528 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1528 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1528 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1528 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52574] The complementary binding of VGAM1528 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1528 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1528 host target RNA into VGAM1528 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52575] It is appreciated that VGAM1528 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1528 host target genes. The mRNA of each one of this plurality of VGAM1528 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1528 RNA, herein designated VGAM

RNA, and which when bound by VGAM1528 RNA causes inhibition of translation of respective one or more VGAM1528 host target proteins.

[52576] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1528 gene, herein designated VGAM GENE, on one or more VGAM1528 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52577] It is yet further appreciated that a function of VGAM1528 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,



utilities of VGAM1528 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1528 correlate with, and may be deduced from, the identity of the host target genes which VGAM1528 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52578] Nucleotide sequences of the VGAM1528 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1528 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1528 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1528 are further described hereinbelow with reference to Table 1.

[52579] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1528 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1528 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52580] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1528 gene, herein designated VGAM is

inhibition of expression of VGAM1528 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1528 correlate with, and may be deduced from, the identity of the target genes which VGAM1528 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52581] Membrane Component, Chromosome 11, Surface Marker 1 (M11S1, Accession NM\_005898) is a VGAM1528 host target gene. M11S1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by M11S1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of M11S1 BINDING SITE, designated SEQ ID:12516, to the nucleotide sequence of VGAM1528 RNA, herein designated VGAM RNA, also designated SEQ ID:4239.

[52582] A function of VGAM1528 is therefore inhibition of Membrane Component, Chromosome 11, Surface Marker 1 (M11S1, Accession NM\_005898), a gene which may play a role in transporting nutrients from the gut lumen across the gutlining epithelial cell layer. Accordingly, utilities of VGAM1528 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with M11S1. The function of M11S1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM131. Placenta-specific 1 (PLAC1, Accession NM\_021796) is another VGAM1528 host target gene. PLAC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAC1 BINDING SITE, designated SEQ ID:22352, to the nucleotide sequence of VGAM1528 RNA, herein designated VGAM RNA, also designated SEQ ID:4239.

[52583] Another function of VGAM1528 is therefore inhibition of Placenta-specific 1 (PLAC1, Accession NM\_021796). Accordingly, utilities of VGAM1528 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAC1. Ubiquitin Protein Ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome) (UBE3A, Accession NM\_130838) is another VGAM1528 host target gene. UBE3A BINDING SITE1

through UBE3A BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UBE3A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE3A BINDING SITE1 through UBE3A BINDING SITE3, designated SEQ ID:28360, SEQ ID:28364 and SEQ ID:6079 respectively, to the nucleotide sequence of VGAM1528 RNA, herein designated VGAM RNA, also designated SEQ ID:4239.

[52584] Another function of VGAM1528 is therefore inhibition of Ubiquitin Protein Ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome) (UBE3A, Accession NM\_130838). Accordingly, utilities of VGAM1528 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE3A. LOC91250 (Accession XM\_037135) is another VGAM1528 host target gene. LOC91250 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91250, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91250 BINDING SITE, desig-

nated SEQ ID:32548, to the nucleotide sequence of VGAM1528 RNA, herein designated VGAM RNA, also designated SEQ ID:4239.

[52585] Another function of VGAM1528 is therefore inhibition of LOC91250 (Accession XM\_037135). Accordingly, utilities of VGAM1528 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91250. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1529 (VGAM1529) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52586] VGAM1529 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1529 was detected is described hereinabove with reference to Figs. 1–8.

[52587] VGAM1529 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus. VGAM1529 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52588] VGAM1529 gene encodes a VGAM1529 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1529 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1529 precursor RNA is designated SEQ ID:1515, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1515 is located at position 69246 relative to the genome of Ectromelia Virus.

[52589] VGAM1529 precursor RNA folds onto itself, forming VGAM1529 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52590] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1529 folded precursor RNA into VGAM1529 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1529 RNA is designated SEQ ID:4240, and is provided hereinbelow with reference to the sequence listing part.

[52591] VGAM1529 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1529 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1529 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52592] VGAM1529 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1529 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1529 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1529 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1529 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52593] The complementary binding of VGAM1529 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1529 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1529 host target RNA into VGAM1529 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52594] It is appreciated that VGAM1529 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1529 host target genes. The mRNA of each one of this plurality of VGAM1529 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1529 RNA, herein designated VGAM RNA, and which when bound by VGAM1529 RNA causes inhibition of translation of respective one or more VGAM1529 host target proteins.

[52595] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1529 gene, herein designated VGAM GENE, on one or more VGAM1529 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[52596] It is yet further appreciated that a function of VGAM1529 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1529 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1529 correlate with, and may be deduced from, the identity of the host target genes which VGAM1529 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52597] Nucleotide sequences of the VGAM1529 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1529 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1529 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1529 are further described hereinbelow with reference to Table 1.

[52598] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1529 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1529 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52599] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1529 gene, herein designated VGAM is inhibition of expression of VGAM1529 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1529 correlate with, and may be deduced from, the identity of the target genes which VGAM1529 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52600] Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542) is a VGAM1529 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45216, to the nucleotide sequence of VGAM1529 RNA, herein designated VGAM RNA, also designated SEQ ID:4240.

[52601] A function of VGAM1529 is therefore inhibition of Hepa-

toocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM1529 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. Chromosome 20 Open Reading Frame 43 (C20orf43, Accession XM\_009549) is another VGAM1529 host target gene. C20orf43 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf43, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf43 BINDING SITE, designated SEQ ID:30113, to the nucleotide sequence of VGAM1529 RNA, herein designated VGAM RNA, also designated SEQ ID:4240.

[52602] Another function of VGAM1529 is therefore inhibition of Chromosome 20 Open Reading Frame 43 (C20orf43, Accession XM\_009549). Accordingly, utilities of VGAM1529

include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf43.

KIAA1559 (Accession XM\_054472) is another VGAM1529 host target gene. KIAA1559 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1559 BINDING SITE, designated SEQ ID:36160, to the nucleotide sequence of VGAM1529 RNA, herein designated VGAM RNA, also designated SEQ ID:4240.

[52603] Another function of VGAM1529 is therefore inhibition of KIAA1559 (Accession XM\_054472). Accordingly, utilities of VGAM1529 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1559. LOC152179 (Accession XM\_098170) is another VGAM1529 host target gene. LOC152179 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC152179 BINDING SITE, designated SEQ ID:41431, to the nucleotide sequence of VGAM1529 RNA, herein designated VGAM RNA, also designated SEQ ID:4240.

[52604] Another function of VGAM1529 is therefore inhibition of LOC152179 (Accession XM\_098170). Accordingly, utilities of VGAM1529 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152179. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1530 (VGAM1530) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52605] VGAM1530 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1530 was detected is described hereinabove with reference to Figs. 1–8.

[52606] VGAM1530 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus. VGAM1530 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52607] VGAM1530 gene encodes a VGAM1530 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1530 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1530 precursor RNA is designated SEQ ID:1516, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1516 is located at position 73081 relative to the genome of Ectromelia Virus.

[52608] VGAM1530 precursor RNA folds onto itself, forming VGAM1530 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52609] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1530 folded precursor RNA into VGAM1530 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1530 RNA is designated SEQ ID:4241, and is provided hereinbelow with reference to the sequence listing part.

[52610] VGAM1530 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1530 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1530 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52611] VGAM1530 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1530 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1530 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-



illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1530 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1530 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52612] The complementary binding of VGAM1530 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1530 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1530 host target RNA into VGAM1530 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52613] It is appreciated that VGAM1530 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1530 host target genes. The mRNA of each one of this plurality of VGAM1530 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1530 RNA, herein designated VGAM RNA, and which when bound by VGAM1530 RNA causes inhibition of translation of respective one or more VGAM1530 host target proteins.

[52614] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1530 gene, herein designated VGAM GENE, on one or more VGAM1530 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[52615] It is yet further appreciated that a function of VGAM1530 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1530 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1530 correlate with, and may be deduced from, the identity of the host target genes which VGAM1530 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52616] Nucleotide sequences of the VGAM1530 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1530 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1530 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1530 are further described hereinbelow with reference to Table 1.

[52617] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1530 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1530 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52618] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1530 gene, herein designated VGAM is inhibition of expression of VGAM1530 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1530 correlate with, and may be deduced from, the identity of the target genes which VGAM1530 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52619] KIAA0429 (Accession NM\_014751) is a VGAM1530 host target gene. KIAA0429 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0429 BINDING SITE, designated SEQ ID:16467, to the nucleotide sequence of VGAM1530 RNA, herein designated VGAM RNA, also designated SEQ ID:4241.

[52620] A function of VGAM1530 is therefore inhibition of

KIAA0429 (Accession NM\_014751). Accordingly, utilities of VGAM1530 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0429. Protocadherin 17 (PCDH17, Accession NM\_014459) is another VGAM1530 host target gene. PCDH17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH17 BINDING SITE, designated SEQ ID:15812, to the nucleotide sequence of VGAM1530 RNA, herein designated VGAM RNA, also designated SEQ ID:4241.

[52621] Another function of VGAM1530 is therefore inhibition of Protocadherin 17 (PCDH17, Accession NM\_014459). Accordingly, utilities of VGAM1530 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH17. LOC256806 (Accession XM\_172865) is another VGAM1530 host target gene. LOC256806 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256806, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256806 BINDING SITE, designated SEQ ID:46143, to the nucleotide sequence of VGAM1530 RNA, herein designated VGAM RNA, also designated SEQ ID:4241.

[52622] Another function of VGAM1530 is therefore inhibition of LOC256806 (Accession XM\_172865). Accordingly, utilities of VGAM1530 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256806. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1531 (VGAM1531) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52623] VGAM1531 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1531 was detected is described hereinabove with reference to Figs. 1–8.

[52624] VGAM1531 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus.

VGAM1531 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52625] VGAM1531 gene encodes a VGAM1531 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1531 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1531 precursor RNA is designated SEQ ID:1517, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1517 is located at position 66901 relative to the genome of Ectromelia Virus.

[52626] VGAM1531 precursor RNA folds onto itself, forming VGAM1531 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52627] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1531 folded precursor RNA into VGAM1531 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1531 RNA is designated SEQ ID:4242, and is provided hereinbelow with reference to the sequence listing part.

[52628] VGAM1531 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1531 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1531 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52629] VGAM1531 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1531 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM1531 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1531 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1531 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52630] The complementary binding of VGAM1531 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1531 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1531 host target RNA into VGAM1531 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52631] It is appreciated that VGAM1531 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1531 host target genes. The mRNA of each one of this plurality of VGAM1531 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1531 RNA, herein designated VGAM RNA, and which when bound by VGAM1531 RNA causes inhibition of translation of respective one or more VGAM1531 host target proteins.

[52632] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1531 gene, herein designated VGAM GENE, on one or more VGAM1531 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52633] It is yet further appreciated that a function of VGAM1531 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1531 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1531 correlate with, and may be deduced from, the identity of the host target genes which VGAM1531 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52634] Nucleotide sequences of the VGAM1531 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1531 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1531 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1531 are further described hereinbelow with reference to Table 1.

[52635] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1531 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1531 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52636] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1531 gene, herein designated VGAM is inhibition of expression of VGAM1531 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1531 correlate with, and may be deduced from, the identity of the target genes which VGAM1531 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52637] Ubiquitin-conjugating Enzyme E2L 3 (UBE2L3, Accession NM\_003347) is a VGAM1531 host target gene. UBE2L3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2L3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2L3 BINDING SITE, designated SEQ ID:9361, to the

nucleotide sequence of VGAM1531 RNA, herein designated VGAM RNA, also designated SEQ ID:4242.

[52638] A function of VGAM1531 is therefore inhibition of Ubiquitin-conjugating Enzyme E2L 3 (UBE2L3, Accession NM\_003347), a gene which catalyzes the covalent attachment of ubiquitin to other proteins. Accordingly, utilities of VGAM1531 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2L3. The function of UBE2L3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM215.ATP-binding Cassette, Sub-family A (ABC1), Member 5 (ABCA5, Accession NM\_018672) is another VGAM1531 host target gene. ABCA5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ABCA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCA5 BINDING SITE, designated SEQ ID:20745, to the nucleotide sequence of VGAM1531 RNA, herein designated VGAM RNA, also designated SEQ ID:4242.

[52639] Another function of VGAM1531 is therefore inhibition of

ATP-binding Cassette, Sub-family A (ABC1), Member 5 (ABCA5, Accession NM\_018672). Accordingly, utilities of VGAM1531 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCA5. DKFZP434B103 (Accession NM\_015644) is another VGAM1531 host target gene. DKFZP434B103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434B103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434B103 BINDING SITE, designated SEQ ID:17895, to the nucleotide sequence of VGAM1531 RNA, herein designated VGAM RNA, also designated SEQ ID:4242.

[52640] Another function of VGAM1531 is therefore inhibition of DKFZP434B103 (Accession NM\_015644). Accordingly, utilities of VGAM1531 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434B103. FLJ13693 (Accession NM\_024807) is another VGAM1531 host target gene. FLJ13693 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13693, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13693 BINDING SITE, designated SEQ ID:24188, to the nucleotide sequence of VGAM1531 RNA, herein designated VGAM RNA, also designated SEQ ID:4242.

[52641] Another function of VGAM1531 is therefore inhibition of FLJ13693 (Accession NM\_024807). Accordingly, utilities of VGAM1531 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13693. FLJ20699 (Accession NM\_017931) is another VGAM1531 host target gene. FLJ20699 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20699, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20699 BINDING SITE, designated SEQ ID:19619, to the nucleotide sequence of VGAM1531 RNA, herein designated VGAM RNA, also designated SEQ ID:4242.

[52642] Another function of VGAM1531 is therefore inhibition of FLJ20699 (Accession NM\_017931). Accordingly, utilities of VGAM1531 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20699. Potassium Voltage-gated Channel, Isk-related Family, Member 4 (KCNE4, Accession NM\_080671) is another VGAM1531 host target gene. KCNE4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNE4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNE4 BINDING SITE, designated SEQ ID:27968, to the nucleotide sequence of VGAM1531 RNA, herein designated VGAM RNA, also designated SEQ ID:4242.

[52643] Another function of VGAM1531 is therefore inhibition of Potassium Voltage-gated Channel, Isk-related Family, Member 4 (KCNE4, Accession NM\_080671). Accordingly, utilities of VGAM1531 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNE4. LOC147976 (Accession XM\_085980) is another VGAM1531 host target gene. LOC147976 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC147976 BINDING SITE, designated SEQ ID:38431, to the nucleotide sequence of VGAM1531 RNA, herein designated VGAM RNA, also designated SEQ ID:4242.

[52644] Another function of VGAM1531 is therefore inhibition of LOC147976 (Accession XM\_085980). Accordingly, utilities of VGAM1531 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147976. LOC51236 (Accession NM\_016458) is another VGAM1531 host target gene. LOC51236 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51236 BINDING SITE, designated SEQ ID:18575, to the nucleotide sequence of VGAM1531 RNA, herein designated VGAM RNA, also designated SEQ ID:4242.

[52645] Another function of VGAM1531 is therefore inhibition of LOC51236 (Accession NM\_016458). Accordingly, utilities of VGAM1531 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51236. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1532 (VGAM1532) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52646] VGAM1532 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1532 was detected is described hereinabove with reference to Figs. 1–8.

[52647] VGAM1532 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1532 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52648] VGAM1532 gene encodes a VGAM1532 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1532 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1532 precursor RNA is designated SEQ ID:1518, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1518 is located at position 83358 relative to the genome of Cowpox Virus.

[52649] VGAM1532 precursor RNA folds onto itself, forming VGAM1532 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52650] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1532 folded precursor RNA into VGAM1532 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1532 RNA is designated SEQ ID:4243, and is provided hereinbelow with reference to the sequence listing part.

[52651] VGAM1532 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1532 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1532 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52652] VGAM1532 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1532 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1532 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1532 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1532 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[52653] The complementary binding of VGAM1532 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1532 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1532 host target RNA into VGAM1532 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52654] It is appreciated that VGAM1532 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1532 host target genes. The mRNA of each one of this plurality of VGAM1532 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1532 RNA, herein designated VGAM RNA, and which when bound by VGAM1532 RNA causes inhibition of translation of respective one or more

VGAM1532 host target proteins.

[52655] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1532 gene, herein designated VGAM GENE, on one or more VGAM1532 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52656] It is yet further appreciated that a function of VGAM1532 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1532 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific

functions, and accordingly utilities, of VGAM1532 correlate with, and may be deduced from, the identity of the host target genes which VGAM1532 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52657] Nucleotide sequences of the VGAM1532 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1532 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1532 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1532 are further described hereinbelow with reference to Table 1.

[52658] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1532 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1532 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52659] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1532 gene, herein designated VGAM is inhibition of expression of VGAM1532 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1532 correlate with, and may be deduced from, the identity of the target genes which VGAM1532 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52660] Dual Specificity Phosphatase 10 (DUSP10, Accession NM\_007207) is a VGAM1532 host target gene. DUSP10 BINDING SITE1 and DUSP10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DUSP10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP10 BINDING SITE1 and DUSP10 BINDING SITE2, designated SEQ ID:14071 and SEQ ID:29555 respectively, to the nucleotide sequence of VGAM1532 RNA, herein designated VGAM RNA, also designated SEQ ID:4243.

[52661] A function of VGAM1532 is therefore inhibition of Dual Specificity Phosphatase 10 (DUSP10, Accession NM\_007207). Accordingly, utilities of VGAM1532 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DUSP10. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to



here as Viral Genomic Address Messenger 1533 (VGAM1533) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52662] VGAM1533 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1533 was detected is described hereinabove with reference to Figs. 1–8.

[52663] VGAM1533 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1533 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52664] VGAM1533 gene encodes a VGAM1533 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1533 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1533 precursor RNA is designated SEQ ID:1519, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1519 is located at position 82024 relative to the genome of Cowpox Virus.

[52665] VGAM1533 precursor RNA folds onto itself, forming VGAM1533 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52666] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1533 folded precursor RNA into VGAM1533 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1533 RNA is designated SEQ ID:4244, and is provided hereinbelow with reference to the sequence listing part.

[52667] VGAM1533 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1533 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1533 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52668] VGAM1533 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1533 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1533 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1533 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1533 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52669] The complementary binding of VGAM1533 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1533 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1533 host target RNA into VGAM1533 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52670] It is appreciated that VGAM1533 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1533 host target genes. The mRNA of each one of this plurality of VGAM1533 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1533 RNA, herein designated VGAM RNA, and which when bound by VGAM1533 RNA causes inhibition of translation of respective one or more VGAM1533 host target proteins.

[52671] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1533 gene, herein designated VGAM GENE, on one or more VGAM1533 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52672] It is yet further appreciated that a function of VGAM1533 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1533 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1533 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52673] Nucleotide sequences of the VGAM1533 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1533 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1533 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1533 are further described hereinbelow with reference to Table 1.

[52674] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1533 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1533 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52675] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1533 gene, herein designated VGAM is inhibition of expression of VGAM1533 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1533 correlate with, and may be deduced from, the identity of the target genes which VGAM1533

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52676] Ceroid–lipofuscinosis, Neuronal 2, Late Infantile (Jansky–Bielschowsky disease) (CLN2, Accession NM\_000391) is a VGAM1533 host target gene. CLN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN2 BINDING SITE, designated SEQ ID:5964, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52677] A function of VGAM1533 is therefore inhibition of Ceroid–lipofuscinosis, Neuronal 2, Late Infantile (Jansky–Bielschowsky disease) (CLN2, Accession NM\_000391). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN2. DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 11 (CHL1–like helicase homolog, *S. cerevisiae*) (DDX11, Accession NM\_030655) is another VGAM1533 host target gene. DDX11 BINDING SITE1 and DDX11 BINDING SITE2 are

HOST TARGET binding sites found in untranslated regions of mRNA encoded by DDX11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX11 BINDING SITE1 and DDX11 BINDING SITE2, designated SEQ ID:24983 and SEQ ID:10651 respectively, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52678] Another function of VGAM1533 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 11 (CHL1–like helicase homolog, *S. cerevisiae*) (DDX11, Accession NM\_030655), a gene which could be an ATP–dependent DNA–binding helicase and may intervene in cell cycle regulation. Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX11. The function of DDX11 has been established by previous studies. Helicases are essential components of a number of multi–protein complexes, including those that regulate transcription, splicing, translation, and DNA repair. These enzymes assist in the unwinding of double–stranded DNA and RNA as an essential part of their function. DEAD box



proteins are putative RNA helicases that have a characteristic Asp-Glu-Ala-Asp (DEAD) box as 1 of 8 highly conserved sequence motifs. See 600396. The yeast Chl1 gene encodes a putative helicase that appears to be essential for normal chromosome transmission. Amann et al.

(1996) studied 2 human genes related to the Chl1 gene of *Saccharomyces cerevisiae*: CHLR1 and CHLR2 (OMIM Ref. No. 601151). The open reading frames (ORFs) of these genes encode proteins with a predicted molecular weight of 102 kD, and the in vitro transcribed and translated products bind efficiently to single-stranded DNA. The predicted ORFs of these 2 genes are more than 98% identical, suggesting that they may have redundant functions. The genes were localized to 12p11 and 12p13 by analysis of somatic cell hybrids and fluorescence in situ hybridization. Fluorescence in situ hybridization indicated that the 2 CHLR gene loci are physically distinct and separated by 8 to 12 Mb. Others had reported the duplication of this region of 12p involving a human expressed sequence tag (EST) and 2 previously uncharacterized cDNAs, which Amann et al. (1996) showed were, in fact, the CHLR genes. A comparison of the CHLR gene sequences with available databases indicated that a large proportion of these

genes, including exons encoding 2 functional domains of the carboxyl-terminal region, had been duplicated as part of a large human telomeric repeat sequence found on many human chromosomes. The results suggested to the authors that duplication of a relatively large region of chromosome 12p containing this putative helicase gene has resulted in the creation of numerous pseudogenes as part of a subtelomeric repeat. Amann et al. (1996) stated that the presence of these helicase pseudogenes, as well as pseudogenes for other genes such as the interleukin-9 receptor (OMIM Ref. No. 300007), within many subtelomeric regions supported the possibility that the spread of this region is subject to exchange between different chromosomes and may have implications for elucidation of the mechanism of intra- and interchromosomal duplication events. Frank and Werner (1996) used differential display PCR to identify novel cDNAs in keratinocytes whose expression is regulated by keratinocyte growth factor (KGF; 148180). One such clone, termed KRG2 by the authors, was identified, and a full-length cDNA was cloned from a KGF-stimulated keratinocyte cDNA library. Southern blot analysis suggested that KRG2 is a member of a multigene family. Northern blot analysis revealed a single 4.3-kb

mRNA whose expression is upregulated by KGF. The authors used RNase protection assays to determine that serum, EGF, and cytokine IL-1-beta (OMIM Ref. No. 147720) had no effect on KRG2 expression, while inhibitors of keratinocyte proliferation, such as TGF-beta-1 (OMIM Ref. No. 190180) and TNF-alpha (OMIM Ref. No. 191160), caused a slight reduction in KRG2 expression. Sequence analysis indicated that the KRG2 cDNA encodes an 856-amino acid protein that is 32% identical to the yeast gene CHL1. Frank and Werner (1996) hypothesized that KRG2 may be involved in cell cycle regulation.

[52679] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52680] Amann, J.; Kidd, V. J.; Lahti, J. M. : Characterization of putative human homologues of the yeast chromosome transmission fidelity gene, CHL1. J. Biol. Chem. 272: 3823-3832, 1997. ; and

[52681] Frank, S.; Werner, S. : The human homologue of the yeast CHL1 gene is a novel keratinocyte growth factor-regulated gene. J. Biol. Chem. 271: 24337-24340, 1996.

[52682] Further studies establishing the function and utilities of DDX11 are found in John Hopkins OMIM database record

ID 601150, and in cited publications numbered 7541–7543 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Epidermal Growth Factor Receptor Pathway Substrate 8 (EPS8, Accession NM\_004447) is another VGAM1533 host target gene. EPS8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EPS8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPS8 BINDING SITE, designated SEQ ID:10743, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52683] Another function of VGAM1533 is therefore inhibition of Epidermal Growth Factor Receptor Pathway Substrate 8 (EPS8, Accession NM\_004447), a gene which has a role in normal and neoplastic cell proliferation; contains an SH3 motif. Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPS8. The function of EPS8 has been established by previous studies. Using an expression cloning approach for the study of epidermal growth factor

(EGF) receptor (EGFR; 131550)–activated signaling, Wong et al. (1994) found a number of murine cDNA clones referred to as eps, for egfr–pathway–substrate. (See 600051 for one of these, EPS15.) One of the clones encoded a protein of 97 kD, designated eps8, which was phosphorylated in vivo by several receptor tyrosine kinases (Fazioli et al., 1993). In addition to a previously identified SH3 domain, Wong et al. (1994) found that the predicted amino acid sequence of human EPS8 showed a nonrandom distribution of prolines, clustered in a way to suggest SH3–binding sites and a putative PH domain. EPS8 was expressed in all epithelial and fibroblast cell lines examined and in some, but not all, hematopoietic cells. An essential function of EPS8 in cell growth regulation was underscored by its conservation during evolution where EPS8–related sequences were detected as early as in *S. cerevisiae*. EGFR signaling involves small GTPases of the Rho family, and EGFR trafficking involves small GTPases of the Rab family. Lanzetti et al. (2000) reported that the EPS8 protein connects these signaling pathways. EPS8 is a substrate of EGFR that is held in a complex with SOS1 by the adaptor protein E3B1, thereby mediating activation of RAC. Through its SH3 domain, EPS8 interacts with RNTRE

(OMIM Ref. No. 605405). Lanzetti et al. (2000) showed that RNTRE is a RAB5 (OMIM Ref. No. 179512) GTPase-activating protein whose activity is regulated by EGFR. By entering in a complex with EPS8, RNTRE acts on RAB5 and inhibits internalization of the EGFR. Furthermore, RNTRE diverts EPS8 from its RAC-activating function, resulting in the attenuation of RAC signaling. Thus, depending on its state of association with E3B1 or RNTRE, EPS8 participates in both EGFR signaling through RAC and EGFR trafficking through RAB5. Wong et al. (1994) mapped the human EPS8 locus to 12q23-q24 by study of human-rodent somatic cell hybrid DNAs and by fluorescence in situ hybridization. In an study of candidate genes for Noonan syndrome (OMIM Ref. No. 163950), Ion et al. (2000) reassigned the map position of EPS8 to 12q13 using FISH.

[52684] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52685] Wong, W. T.; Carlomagno, F.; Druck, T.; Barletta, C.; Croce, C. M.; Huebner, K.; Kraus, M. H.; Di Fiore, P. P. : Evolutionary conservation of the EPS8 gene and its mapping to human chromosome 12q23-q24. *Oncogene* 9: 3057-3061, 1994. ; and

[52686] Lanzetti, L.; Rybin, V.; Malabarba, M. G.; Christoforidis, S.; Scita, G.; Zerial, M.; Di Fiore, P. P. : The Eps8 protein coordinates EGF receptor signalling through Rac and trafficking t.

[52687] Further studies establishing the function and utilities of EPS8 are found in John Hopkins OMIM database record ID 600206, and in cited publications numbered 1591, 199 and 2125 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Coagulation Factor VII (serum prothrombin conversion accelerator) (F7, Accession NM\_019616) is another VGAM1533 host target gene. F7 BINDING SITE1 and F7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by F7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F7 BINDING SITE1 and F7 BINDING SITE2, designated SEQ ID:21237 and SEQ ID:5608 respectively, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52688] Another function of VGAM1533 is therefore inhibition of Coagulation Factor VII (serum prothrombin conversion ac-

celerator) (F7, Accession NM\_019616). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F7. Fragile X Mental Retardation 1 (FMR1, Accession NM\_002024) is another VGAM1533 host target gene. FMR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FMR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FMR1 BINDING SITE, designated SEQ ID:7775, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52689] Another function of VGAM1533 is therefore inhibition of Fragile X Mental Retardation 1 (FMR1, Accession NM\_002024). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FMR1. LFG (Accession XM\_084780) is another VGAM1533 host target gene. LFG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LFG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-



trates the complementarity of the nucleotide sequences of LFG BINDING SITE, designated SEQ ID:37687, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52690] Another function of VGAM1533 is therefore inhibition of LFG (Accession XM\_084780). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LFG. Orthodenticle Homolog 1 (Drosophila) (OTX1, Accession NM\_014562) is another VGAM1533 host target gene. OTX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OTX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OTX1 BINDING SITE, designated SEQ ID:15898, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52691] Another function of VGAM1533 is therefore inhibition of Orthodenticle Homolog 1 (Drosophila) (OTX1, Accession NM\_014562), a gene which plays a role in the development of the brain and the sense organs. Accordingly, utilities of VGAM1533 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with OTX1. The function of OTX1 has been established by previous studies. OTX1 is a homeobox family gene related to a gene expressed in the developing *Drosophila* head termed 'orthodenticle.' Simeone et al. (1992) identified rodent OTX2 (OMIM Ref. No. 600037). A homolog is also found in the zebrafish. Tissue expression of OTX1 is similar to that of OTX2 but is more restricted (Boncinelli et al., 1993). Frantz et al. (1994) showed that *Otx1* mRNA was expressed by precursors of deep-layer neurons within cortical layers 5 and 6 of the rat brain during both postnatal and adult life. Using a cosmid containing the gene, Kastury et al. (1994) mapped human OTX1 to 2p13 by fluorescence in situ hybridization, near the locus for EMX1 (OMIM Ref. No. 600034). Animal model experiments lend further support to the function of OTX1. Acampora et al. (1996) produced null mice by replacing *Otx1* with the lacZ gene. *Otx* <sup>-/-</sup> mice exhibited epileptic behavior with the characteristics of both focal and generalized seizures. Anatomic and histologic analyses of brains from 2-4-month-old *Otx* <sup>-/-</sup> mice revealed multiple abnormalities affecting mainly the telencephalic, temporal, and perirhinal areas, the hippocampus, mesencephalon, and

cerebellum, and the acoustic and visual sense organs. Acampora et al. (1996) reported that in older Otx  $-/-$  mice the epileptic behavior and frequency of seizures were somewhat reduced, although they never disappeared. They detected neither epileptic behavior nor electrical seizures in Otx $+/(-)$  mice. The authors stated that this study provides the first evidence that loss of function of a homeobox-containing gene affects brain development and induces spontaneous epilepsy.

[52692] It is appreciated that the abovementioned animal model for OTX1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[52693] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52694] Frantz, G. D.; Weimann, J. M.; Levin, M. E.; McConnell, S. K. : Otx1 and Otx2 define layers and regions in developing cerebral cortex and cerebellum. J. Neurosci. 14: 5725–5740, 1994. ; and

[52695] Acampora, D.; Mazan, S.; Avantaggiato, V.; Barone, P.; Tuorto, F.; Lallemand, Y.; Brulet, P.; Simeone, A. : Epilepsy and brain abnormalities in mice lacking the Otx1 gene.

Nature Genet.

[52696] Further studies establishing the function and utilities of OTX1 are found in John Hopkins OMIM database record ID 600036, and in cited publications numbered 8116–811 and 8110–8111 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Synaptosomal–associated Protein, 23kDa (SNAP23, Accession NM\_003825) is another VGAM1533 host target gene. SNAP23 BINDING SITE1 and SNAP23 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SNAP23, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAP23 BINDING SITE1 and SNAP23 BINDING SITE2, designated SEQ ID:9919 and SEQ ID:28284 respectively, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52697] Another function of VGAM1533 is therefore inhibition of Synaptosomal–associated Protein, 23kDa (SNAP23, Accession NM\_003825), a gene which is essential component of the high affinity receptor for the general membrane fusion machinery. Accordingly, utilities of VGAM1533 include di–

agnosis, prevention and treatment of diseases and clinical conditions associated with SNAP23. The function of SNAP23 has been established by previous studies. Synaptosomal-associated proteins (SNAPs) are involved in the process of membrane fusion in intracellular vesicle traffic. By fluorescence in situ hybridization, Lazo et al. (2001) mapped the SNAP23 gene to chromosome 15q21-q22. Lazo et al. (2001) suggested that alterations in the SNAP23 gene may be involved in neurologic and other diseases with defects in vesicle-membrane fusion processes that map to 15q15-q21.

[52698] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[52699] Lazo, P. A.; Nadal, M.; Ferrer, M.; Area, E.; Hernandez-Torres, J.; Nabokina, S. M.; Mollinedo, F.; Estivill, X. : Genomic organization, chromosomal localization, alternative splicing, and isoforms of the human synaptosome-associated protein-23 gene implicated in vesicle-membrane fusion processes. Hum. Genet. 108: 211-215, 2001. ; and

[52700] Mollinedo, F.; Lazo, P. A. : Identification of two isoforms of the vesicle-membrane fusion protein SNAP-23 in human neutrophils and HL-60 cells. Biochem. Biophys. Res. Com-

mun. 231: 808.

[52701] Further studies establishing the function and utilities of SNAP23 are found in John Hopkins OMIM database record ID 602534, and in cited publications numbered 8872–8876 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. A Kinase (PRKA) Anchor Protein (gravin) 12 (AKAP12, Accession NM\_005100) is another VGAM1533 host target gene. AKAP12 BINDING SITE1 and AKAP12 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AKAP12, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP12 BINDING SITE1 and AKAP12 BINDING SITE2, designated SEQ ID:11572 and SEQ ID:29312 respectively, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52702] Another function of VGAM1533 is therefore inhibition of A Kinase (PRKA) Anchor Protein (gravin) 12 (AKAP12, Accession NM\_005100). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP12. DEAD/H

(Asp-Glu-Ala-Asp/His) Box Polypeptide 12 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX12, Accession XM\_006936) is another VGAM1533 host target gene. DDX12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX12 BINDING SITE, designated SEQ ID:30021, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52703] Another function of VGAM1533 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 12 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX12, Accession XM\_006936). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX12. ERO1-like (*S. cerevisiae*) (ERO1L, Accession NM\_014584) is another VGAM1533 host target gene. ERO1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERO1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERO1L BINDING SITE, designated SEQ ID:15940, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52704] Another function of VGAM1533 is therefore inhibition of ERO1-like (*S. cerevisiae*) (ERO1L, Accession NM\_014584). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERO1L. FLJ11413 (Accession NM\_024554) is another VGAM1533 host target gene. FLJ11413 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11413 BINDING SITE, designated SEQ ID:23772, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52705] Another function of VGAM1533 is therefore inhibition of FLJ11413 (Accession NM\_024554). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment



of diseases and clinical conditions associated with FLJ11413. FLJ20040 (Accession NM\_018992) is another VGAM1533 host target gene. FLJ20040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20040 BINDING SITE, designated SEQ ID:21066, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52706] Another function of VGAM1533 is therefore inhibition of FLJ20040 (Accession NM\_018992). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20040. FLJ20772 (Accession NM\_017956) is another VGAM1533 host target gene. FLJ20772 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20772 BINDING SITE, designated SEQ ID:19665, to the nucleotide

sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52707] Another function of VGAM1533 is therefore inhibition of FLJ20772 (Accession NM\_017956). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20772. FLJ30574 (Accession NM\_144629) is another VGAM1533 host target gene. FLJ30574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30574 BINDING SITE, designated SEQ ID:29447, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52708] Another function of VGAM1533 is therefore inhibition of FLJ30574 (Accession NM\_144629). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30574. FLJ31168 (Accession NM\_144712) is another VGAM1533 host target gene. FLJ31168 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ31168, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31168 BINDING SITE, designated SEQ ID:29536, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52709] Another function of VGAM1533 is therefore inhibition of FLJ31168 (Accession NM\_144712). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31168. G Antigen, Family D, 3 (GAGED3, Accession NM\_130777) is another VGAM1533 host target gene. GAGED3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GAGED3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAGED3 BINDING SITE, designated SEQ ID:28268, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52710] Another function of VGAM1533 is therefore inhibition of G

Antigen, Family D, 3 (GAGED3, Accession NM\_130777). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAGED3. IDI2 (Accession NM\_033261) is another VGAM1533 host target gene. IDI2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IDI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IDI2 BINDING SITE, designated SEQ ID:27091, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52711] Another function of VGAM1533 is therefore inhibition of IDI2 (Accession NM\_033261). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IDI2. IPLA2(GAMMA) (Accession XM\_027224) is another VGAM1533 host target gene. IPLA2(GAMMA) BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IPLA2(GAMMA), corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates

the complementarity of the nucleotide sequences of IPLA2(GAMMA) BINDING SITE, designated SEQ ID:30444, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52712] Another function of VGAM1533 is therefore inhibition of IPLA2(GAMMA) (Accession XM\_027224). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IPLA2(GAMMA). KIAA0737 (Accession NM\_014828) is another VGAM1533 host target gene. KIAA0737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0737 BINDING SITE, designated SEQ ID:16820, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52713] Another function of VGAM1533 is therefore inhibition of KIAA0737 (Accession NM\_014828). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0737. KIAA0870 (Accession XM\_088315) is another

VGAM1533 host target gene. KIAA0870 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0870 BINDING SITE, designated SEQ ID:39609, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52714] Another function of VGAM1533 is therefore inhibition of KIAA0870 (Accession XM\_088315). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0870. KIAA1028 (Accession XM\_166324) is another VGAM1533 host target gene. KIAA1028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1028 BINDING SITE, designated SEQ ID:44160, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52715] Another function of VGAM1533 is therefore inhibition of KIAA1028 (Accession XM\_166324). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1028. KIAA1357 (Accession XM\_050421) is another VGAM1533 host target gene. KIAA1357 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1357, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1357 BINDING SITE, designated SEQ ID:35629, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52716] Another function of VGAM1533 is therefore inhibition of KIAA1357 (Accession XM\_050421). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1357. KIAA1617 (Accession XM\_166140) is another VGAM1533 host target gene. KIAA1617 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1617, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1617 BINDING SITE, designated SEQ ID:43941, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52717] Another function of VGAM1533 is therefore inhibition of KIAA1617 (Accession XM\_166140). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1617. Lipoma HMGIC Fusion Partner-like 2 (LHFPL2, Accession XM\_046054) is another VGAM1533 host target gene. LHFPL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LHFPL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LHFPL2 BINDING SITE, designated SEQ ID:34660, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52718] Another function of VGAM1533 is therefore inhibition of Lipoma HMGIC Fusion Partner-like 2 (LHFPL2, Accession XM\_046054). Accordingly, utilities of VGAM1533 include



diagnosis, prevention and treatment of diseases and clinical conditions associated with LHFPL2. Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010) is another VGAM1533 host target gene. MAP2K4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP2K4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K4 BINDING SITE, designated SEQ ID:8914, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52719] Another function of VGAM1533 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K4. PC2 (positive cofactor 2, multiprotein complex) Glutamine/Q-rich-associated Protein (PCQAP, Accession NM\_015889) is another VGAM1533 host target gene. PCQAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCQAP, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCQAP BINDING SITE, designated SEQ ID:18031, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52720] Another function of VGAM1533 is therefore inhibition of PC2 (positive cofactor 2, multiprotein complex) Glutamine/Q-rich-associated Protein (PCQAP, Accession NM\_015889). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCQAP. PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession NM\_005975) is another VGAM1533 host target gene. PTK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTK6 BINDING SITE, designated SEQ ID:12597, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52721] Another function of VGAM1533 is therefore inhibition of PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession

NM\_005975). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTK6. RODH-4 (Accession NM\_003708) is another VGAM1533 host target gene.

RODH-4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RODH-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RODH-4 BINDING SITE, designated SEQ ID:9809, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52722] Another function of VGAM1533 is therefore inhibition of RODH-4 (Accession NM\_003708). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RODH-4. Testis Specific, 14 (TSGA14, Accession NM\_018718) is another VGAM1533 host target gene. TSGA14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSGA14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of TSGA14 BINDING SITE, designated SEQ ID:20794, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52723] Another function of VGAM1533 is therefore inhibition of Testis Specific, 14 (TSGA14, Accession NM\_018718). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSGA14. Wingless-type MMTV Integration Site Family, Member 16 (WNT16, Accession NM\_057168) is another VGAM1533 host target gene. WNT16 BINDING SITE1 and WNT16 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WNT16, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT16 BINDING SITE1 and WNT16 BINDING SITE2, designated SEQ ID:27674 and SEQ ID:18170 respectively, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52724] Another function of VGAM1533 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 16

(WNT16, Accession NM\_057168). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT16. LOC144373 (Accession XM\_084841) is another VGAM1533 host target gene. LOC144373 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144373 BINDING SITE, designated SEQ ID:37726, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52725] Another function of VGAM1533 is therefore inhibition of LOC144373 (Accession XM\_084841). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144373. LOC146728 (Accession XM\_097074) is another VGAM1533 host target gene. LOC146728 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146728, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC146728 BINDING SITE, designated SEQ ID:40723, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52726] Another function of VGAM1533 is therefore inhibition of LOC146728 (Accession XM\_097074). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146728. LOC149566 (Accession XM\_097670) is another VGAM1533 host target gene. LOC149566 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149566 BINDING SITE, designated SEQ ID:41016, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52727] Another function of VGAM1533 is therefore inhibition of LOC149566 (Accession XM\_097670). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149566. LOC150113 (Accession XM\_104532) is an-

other VGAM1533 host target gene. LOC150113 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150113 BINDING SITE, designated SEQ ID:42167, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52728] Another function of VGAM1533 is therefore inhibition of LOC150113 (Accession XM\_104532). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150113. LOC151414 (Accession XM\_087197) is another VGAM1533 host target gene. LOC151414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151414 BINDING SITE, designated SEQ ID:39109, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52729] Another function of VGAM1533 is therefore inhibition of LOC151414 (Accession XM\_087197). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151414. LOC158427 (Accession NM\_139246) is another VGAM1533 host target gene. LOC158427 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158427 BINDING SITE, designated SEQ ID:29246, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52730] Another function of VGAM1533 is therefore inhibition of LOC158427 (Accession NM\_139246). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158427. LOC197196 (Accession XM\_117003) is another VGAM1533 host target gene. LOC197196 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197196, corresponding to a HOST TARGET binding site such as BIND-



ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197196 BINDING SITE, designated SEQ ID:43199, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52731] Another function of VGAM1533 is therefore inhibition of LOC197196 (Accession XM\_117003). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197196. LOC199699 (Accession XM\_113990) is another VGAM1533 host target gene. LOC199699 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199699, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199699 BINDING SITE, designated SEQ ID:42594, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52732] Another function of VGAM1533 is therefore inhibition of LOC199699 (Accession XM\_113990). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC199699. LOC219401 (Accession XM\_166706) is another VGAM1533 host target gene. LOC219401 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219401 BINDING SITE, designated SEQ ID:44591, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52733] Another function of VGAM1533 is therefore inhibition of LOC219401 (Accession XM\_166706). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219401. LOC256112 (Accession XM\_172829) is another VGAM1533 host target gene. LOC256112 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256112 BINDING SITE, designated SEQ ID:46103, to the nucleotide sequence of VGAM1533 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4244.

[52734] Another function of VGAM1533 is therefore inhibition of LOC256112 (Accession XM\_172829). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256112. LOC91464 (Accession XM\_038589) is another VGAM1533 host target gene. LOC91464 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91464 BINDING SITE, designated SEQ ID:32876, to the nucleotide sequence of VGAM1533 RNA, herein designated VGAM RNA, also designated SEQ ID:4244.

[52735] Another function of VGAM1533 is therefore inhibition of LOC91464 (Accession XM\_038589). Accordingly, utilities of VGAM1533 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91464. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1534 (VGAM1534) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52736] VGAM1534 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1534 was detected is described hereinabove with reference to Figs. 1–8.

[52737] VGAM1534 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1534 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52738] VGAM1534 gene encodes a VGAM1534 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1534 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1534 precursor RNA is designated SEQ ID:1520, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1520 is located at position 80718 relative to the genome of Cowpox Virus.

[52739] VGAM1534 precursor RNA folds onto itself, forming

VGAM1534 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52740] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1534 folded precursor RNA into VGAM1534 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM1534 RNA is designated SEQ ID:4245, and is provided hereinbelow with reference to the sequence listing part.

[52741] VGAM1534 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1534 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1534 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52742] VGAM1534 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1534 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1534 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1534 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1534 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52743] The complementary binding of VGAM1534 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1534 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1534 host target RNA into VGAM1534 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52744] It is appreciated that VGAM1534 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1534 host target genes. The mRNA of each one of this plurality of VGAM1534 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1534 RNA, herein designated VGAM RNA, and which when bound by VGAM1534 RNA causes inhibition of translation of respective one or more VGAM1534 host target proteins.

[52745] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1534 gene, herein designated VGAM GENE, on one or more VGAM1534 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52746] It is yet further appreciated that a function of VGAM1534 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1534 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1534 correlate with, and may be deduced from, the identity of the host target genes which VGAM1534 binds and inhibits,



and the function of these host target genes, as elaborated hereinbelow.

[52747] Nucleotide sequences of the VGAM1534 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1534 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1534 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1534 are further described hereinbelow with reference to Table 1.

[52748] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1534 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1534 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52749] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1534 gene, herein designated VGAM is inhibition of expression of VGAM1534 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1534 correlate with, and may be deduced from, the identity of the target genes which VGAM1534 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[52750] Microtubule-associated Protein 1A (MAP1A, Accession NM\_002373) is a VGAM1534 host target gene. MAP1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP1A BINDING SITE, designated SEQ ID:8181, to the nucleotide sequence of VGAM1534 RNA, herein designated VGAM RNA, also designated SEQ ID:4245.

[52751] A function of VGAM1534 is therefore inhibition of Microtubule-associated Protein 1A (MAP1A, Accession NM\_002373), a gene which is a structural protein involved in the filamentous cross-bridging between microtubules and other skeletal elements. Accordingly, utilities of VGAM1534 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP1A. The function of MAP1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM315.MGC20253 (Accession NM\_144583) is another VGAM1534 host target gene. MGC20253 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC20253, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20253 BINDING SITE, designated SEQ ID:29394, to the nucleotide sequence of VGAM1534 RNA, herein designated VGAM RNA, also designated SEQ ID:4245.

[52752] Another function of VGAM1534 is therefore inhibition of MGC20253 (Accession NM\_144583). Accordingly, utilities of VGAM1534 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20253. LOC120856 (Accession XM\_058509) is another VGAM1534 host target gene. LOC120856 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC120856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120856 BINDING SITE, designated SEQ ID:36635, to the nucleotide sequence of VGAM1534 RNA, herein designated VGAM RNA, also designated SEQ ID:4245.

[52753] Another function of VGAM1534 is therefore inhibition of

LOC120856 (Accession XM\_058509). Accordingly, utilities of VGAM1534 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120856. LOC143425 (Accession XM\_113695) is another VGAM1534 host target gene. LOC143425 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143425 BINDING SITE, designated SEQ ID:42347, to the nucleotide sequence of VGAM1534 RNA, herein designated VGAM RNA, also designated SEQ ID:4245.

[52754] Another function of VGAM1534 is therefore inhibition of LOC143425 (Accession XM\_113695). Accordingly, utilities of VGAM1534 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143425. LOC201685 (Accession XM\_117325) is another VGAM1534 host target gene. LOC201685 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201685, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC201685 BINDING SITE, designated SEQ ID:43385, to the nucleotide sequence of VGAM1534 RNA, herein designated VGAM RNA, also designated SEQ ID:4245.

[52755] Another function of VGAM1534 is therefore inhibition of LOC201685 (Accession XM\_117325). Accordingly, utilities of VGAM1534 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201685. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1535 (VGAM1535) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52756] VGAM1535 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1535 was detected is described hereinabove with reference to Figs. 1–8.

[52757] VGAM1535 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus.

VGAM1535 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[52758] VGAM1535 gene encodes a VGAM1535 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1535 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1535 precursor RNA is designated SEQ ID:1521, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1521 is located at position 80457 relative to the genome of Cowpox Virus.

[52759] VGAM1535 precursor RNA folds onto itself, forming VGAM1535 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52760] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1535 folded precursor RNA into VGAM1535 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide sequence of VGAM1535 RNA is designated SEQ ID:4246, and is provided hereinbelow with reference to the sequence listing part.

[52761] VGAM1535 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1535 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1535 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52762] VGAM1535 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1535 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1535 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1535 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1535 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52763] The complementary binding of VGAM1535 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1535 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1535 host target RNA into VGAM1535 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[52764] It is appreciated that VGAM1535 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1535 host target genes. The mRNA of each one of this plurality of VGAM1535 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1535 RNA, herein designated VGAM RNA, and which when bound by VGAM1535 RNA causes inhibition of translation of respective one or more VGAM1535 host target proteins.

[52765] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1535 gene, herein designated VGAM GENE, on one or more VGAM1535 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52766] It is yet further appreciated that a function of VGAM1535 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1535 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1535 correlate with, and may be deduced from, the identity of the host target genes which VGAM1535 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52767] Nucleotide sequences of the VGAM1535 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1535 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1535 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1535 are further described hereinbelow with reference to Table 1.

[52768] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1535 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1535 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52769] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1535 gene, herein designated VGAM is inhibition of expression of VGAM1535 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1535 correlate with, and may be deduced from, the identity of the target genes which VGAM1535 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52770] Potassium Voltage-gated Channel, Shal-related Subfamily, Member 2 (KCND2, Accession NM\_012281) is a VGAM1535 host target gene. KCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCND2 BINDING SITE, designated SEQ ID:14605, to the nucleotide sequence of VGAM1535 RNA, herein designated VGAM RNA,

also designated SEQ ID:4246.

[52771] A function of VGAM1535 is therefore inhibition of Potassium Voltage-gated Channel, Shal-related Subfamily, Member 2 (KCND2, Accession NM\_012281), a gene which is prominent in the repolarization phase of the action potential. Accordingly, utilities of VGAM1535 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCND2. The function of KCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM449. Peripheral Myelin Protein 2 (PMP2, Accession NM\_002677) is another VGAM1535 host target gene.

PMP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMP2 BINDING SITE, designated SEQ ID:8542, to the nucleotide sequence of VGAM1535 RNA, herein designated VGAM RNA, also designated SEQ ID:4246.

[52772] Another function of VGAM1535 is therefore inhibition of Peripheral Myelin Protein 2 (PMP2, Accession

NM\_002677), a gene which is a lipid transport protein in schwann cells. Accordingly, utilities of VGAM1535 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMP2. The function of PMP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. KIAA1229 (Accession XM\_030665) is another VGAM1535 host target gene. KIAA1229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1229 BINDING SITE, designated SEQ ID:31093, to the nucleotide sequence of VGAM1535 RNA, herein designated VGAM RNA, also designated SEQ ID:4246.

[52773] Another function of VGAM1535 is therefore inhibition of KIAA1229 (Accession XM\_030665). Accordingly, utilities of VGAM1535 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1229. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1536 (VGAM1536) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52774] VGAM1536 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1536 was detected is described hereinabove with reference to Figs. 1–8.

[52775] VGAM1536 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1536 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52776] VGAM1536 gene encodes a VGAM1536 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1536 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1536 precursor RNA is designated SEQ ID:1522, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1522 is located at position 77166 relative to the

genome of Cowpox Virus.

[52777] VGAM1536 precursor RNA folds onto itself, forming VGAM1536 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52778] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1536 folded precursor RNA into VGAM1536 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1536 RNA is designated SEQ ID:4247, and is provided hereinbelow with reference to the sequence listing part.

[52779] VGAM1536 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1536 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1536 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[52780] VGAM1536 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1536 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1536 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1536 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1536 host target RNA, herein designated VGAM HOST TARGET RNA. It is further



appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[52781] The complementary binding of VGAM1536 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1536 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1536 host target RNA into VGAM1536 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52782] It is appreciated that VGAM1536 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1536 host target genes. The mRNA of each one of this plurality of VGAM1536 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1536 RNA, herein designated VGAM RNA, and which when bound by VGAM1536 RNA causes inhibition of translation of respective one or more VGAM1536 host target proteins.

[52783] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1536 gene, herein designated VGAM GENE, on one or more VGAM1536 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52784] It is yet further appreciated that a function of VGAM1536 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1536 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1536 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1536 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52785] Nucleotide sequences of the VGAM1536 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1536 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1536 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1536 are further described hereinbelow with reference to Table 1.

[52786] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1536 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1536 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52787] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1536 gene, herein designated VGAM is inhibition of expression of VGAM1536 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1536 correlate with, and may be deduced

from, the identity of the target genes which VGAM1536 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52788] Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542) is a VGAM1536 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45216, to the nucleotide sequence of VGAM1536 RNA, herein designated VGAM RNA, also designated SEQ ID:4247.

[52789] A function of VGAM1536 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM1536 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM174. Chromosome 20 Open Reading Frame 43 (C20orf43, Accession XM\_009549) is another VGAM1536 host target gene. C20orf43 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf43, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf43 BINDING SITE, designated SEQ ID:30113, to the nucleotide sequence of VGAM1536 RNA, herein designated VGAM RNA, also designated SEQ ID:4247.

[52790] Another function of VGAM1536 is therefore inhibition of Chromosome 20 Open Reading Frame 43 (C20orf43, Accession XM\_009549). Accordingly, utilities of VGAM1536 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf43.

KIAA1559 (Accession XM\_054472) is another VGAM1536 host target gene. KIAA1559 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1559 BINDING SITE,

designated SEQ ID:36160, to the nucleotide sequence of VGAM1536 RNA, herein designated VGAM RNA, also designated SEQ ID:4247.

[52791] Another function of VGAM1536 is therefore inhibition of KIAA1559 (Accession XM\_054472). Accordingly, utilities of VGAM1536 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1559. LOC152179 (Accession XM\_098170) is another VGAM1536 host target gene. LOC152179 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152179 BINDING SITE, designated SEQ ID:41431, to the nucleotide sequence of VGAM1536 RNA, herein designated VGAM RNA, also designated SEQ ID:4247.

[52792] Another function of VGAM1536 is therefore inhibition of LOC152179 (Accession XM\_098170). Accordingly, utilities of VGAM1536 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152179. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1537 (VGAM1537) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52793] VGAM1537 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1537 was detected is described hereinabove with reference to Figs. 1–8.

[52794] VGAM1537 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1537 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52795] VGAM1537 gene encodes a VGAM1537 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1537 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1537 precursor RNA is designated SEQ ID:1523, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1523 is located at position 78285 relative to the

genome of Cowpox Virus.

[52796] VGAM1537 precursor RNA folds onto itself, forming VGAM1537 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52797] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1537 folded precursor RNA into VGAM1537 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1537 RNA is designated SEQ ID:4248, and is provided hereinbelow with reference to the sequence listing part.

[52798] VGAM1537 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1537 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1537 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[52799] VGAM1537 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1537 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1537 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1537 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1537 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[52800] The complementary binding of VGAM1537 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1537 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1537 host target RNA into VGAM1537 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52801] It is appreciated that VGAM1537 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1537 host target genes. The mRNA of each one of this plurality of VGAM1537 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1537 RNA, herein designated VGAM RNA, and which when bound by VGAM1537 RNA causes inhibition of translation of respective one or more VGAM1537 host target proteins.

[52802] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1537 gene, herein designated VGAM GENE, on one or more VGAM1537 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52803] It is yet further appreciated that a function of VGAM1537 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1537 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1537 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52804] Nucleotide sequences of the VGAM1537 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1537 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1537 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1537 are further described hereinbelow with reference to Table 1.

[52805] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1537 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1537 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52806] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1537 gene, herein designated VGAM is inhibition of expression of VGAM1537 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1537 correlate with, and may be deduced

from, the identity of the target genes which VGAM1537 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52807] Apical Protein-like (*Xenopus laevis*) (APXL, Accession NM\_001649) is a VGAM1537 host target gene. APXL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APXL BINDING SITE, designated SEQ ID:7352, to the nucleotide sequence of VGAM1537 RNA, herein designated VGAM RNA, also designated SEQ ID:4248.

[52808] A function of VGAM1537 is therefore inhibition of Apical Protein-like (*Xenopus laevis*) (APXL, Accession NM\_001649), a gene which is implicated in amiloride-sensitive sodium channel activity. Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APXL. The function of APXL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152.Cockayne Syndrome 1 (classical) (CKN1, Ac-

cession NM\_000082) is another VGAM1537 host target gene. CKN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKN1 BINDING SITE, designated SEQ ID:5529, to the nucleotide sequence of VGAM1537 RNA, herein designated VGAM RNA, also designated SEQ ID:4248.

[52809] Another function of VGAM1537 is therefore inhibition of Cockayne Syndrome 1 (classical) (CKN1, Accession NM\_000082). Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKN1. High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483) is another VGAM1537 host target gene. HMGA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGA2 BINDING SITE, designated SEQ ID:9561, to the nucleotide sequence of VGAM1537 RNA, herein designated VGAM

RNA, also designated SEQ ID:4248.

[52810] Another function of VGAM1537 is therefore inhibition of High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483), a gene which may affect transcription and cell differentiation; shares common DNA-binding motif with other HMG HMG I/Y family members. Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGA2. The function of HMGA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Zinc Finger Protein 36 (K0X18) (ZNF36, Accession XM\_168302) is another VGAM1537 host target gene. ZNF36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF36 BINDING SITE, designated SEQ ID:45101, to the nucleotide sequence of VGAM1537 RNA, herein designated VGAM RNA, also designated SEQ ID:4248.

[52811] Another function of VGAM1537 is therefore inhibition of

Zinc Finger Protein 36 (K0X 18) (ZNF36, Accession XM\_168302), a gene which may be involved in transcriptional regulation. Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF36. The function of ZNF36 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM804.FLJ23191 (Accession NM\_024574) is another VGAM1537 host target gene. FLJ23191 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23191 BINDING SITE, designated SEQ ID:23803, to the nucleotide sequence of VGAM1537 RNA, herein designated VGAM RNA, also designated SEQ ID:4248.

[52812] Another function of VGAM1537 is therefore inhibition of FLJ23191 (Accession NM\_024574). Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23191. KIAA0841 (Accession XM\_049237) is another



VGAM1537 host target gene. KIAA0841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0841 BINDING SITE, designated SEQ ID:35359, to the nucleotide sequence of VGAM1537 RNA, herein designated VGAM RNA, also designated SEQ ID:4248.

[52813] Another function of VGAM1537 is therefore inhibition of KIAA0841 (Accession XM\_049237). Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0841. Ring Finger Protein 20 (RNF20, Accession NM\_019592) is another VGAM1537 host target gene. RNF20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF20 BINDING SITE, designated SEQ ID:21213, to the nucleotide sequence of VGAM1537 RNA, herein designated VGAM RNA, also designated SEQ

ID:4248.

[52814] Another function of VGAM1537 is therefore inhibition of Ring Finger Protein 20 (RNF20, Accession NM\_019592). Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF20. LOC118851 (Accession XM\_061180) is another VGAM1537 host target gene. LOC118851 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC118851, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118851 BINDING SITE, designated SEQ ID:37199, to the nucleotide sequence of VGAM1537 RNA, herein designated VGAM RNA, also designated SEQ ID:4248.

[52815] Another function of VGAM1537 is therefore inhibition of LOC118851 (Accession XM\_061180). Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118851. LOC150005 (Accession XM\_097795) is another VGAM1537 host target gene. LOC150005 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC150005, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150005 BINDING SITE, designated SEQ ID:41122, to the nucleotide sequence of VGAM1537 RNA, herein designated VGAM RNA, also designated SEQ ID:4248.

[52816] Another function of VGAM1537 is therefore inhibition of LOC150005 (Accession XM\_097795). Accordingly, utilities of VGAM1537 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150005. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1538 (VGAM1538) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52817] VGAM1538 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1538 was detected is described hereinabove with reference to Figs. 1-8.

[52818] VGAM1538 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Monkeypox Virus.

VGAM1538 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52819] VGAM1538 gene encodes a VGAM1538 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1538 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1538 precursor RNA is designated SEQ ID:1524, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1524 is located at position 59766 relative to the genome of Monkeypox Virus.

[52820] VGAM1538 precursor RNA folds onto itself, forming VGAM1538 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52821] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1538 folded precursor RNA into VGAM1538 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1538 RNA is designated SEQ ID:4249, and is provided hereinbelow with reference to the sequence listing part.

[52822] VGAM1538 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1538 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1538 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52823] VGAM1538 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1538 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1538 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1538 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1538 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52824] The complementary binding of VGAM1538 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1538 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1538

host target RNA into VGAM1538 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52825] It is appreciated that VGAM1538 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1538 host target genes. The mRNA of each one of this plurality of VGAM1538 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1538 RNA, herein designated VGAM RNA, and which when bound by VGAM1538 RNA causes inhibition of translation of respective one or more VGAM1538 host target proteins.

[52826] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1538 gene, herein designated VGAM GENE, on one or more VGAM1538 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52827] It is yet further appreciated that a function of VGAM1538 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1538 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1538 correlate with, and may be deduced from, the identity of the host target genes which VGAM1538 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52828] Nucleotide sequences of the VGAM1538 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1538 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1538 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1538 are further



described hereinbelow with reference to Table 1.

[52829] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1538 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1538 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52830] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1538 gene, herein designated VGAM is inhibition of expression of VGAM1538 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1538 correlate with, and may be deduced from, the identity of the target genes which VGAM1538 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52831] Chloride Channel 4 (CLCN4, Accession NM\_001830) is a VGAM1538 host target gene. CLCN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLCN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN4 BINDING SITE,

designated SEQ ID:7569, to the nucleotide sequence of VGAM1538 RNA, herein designated VGAM RNA, also designated SEQ ID:4249.

[52832] A function of VGAM1538 is therefore inhibition of Chloride Channel 4 (CLCN4, Accession NM\_001830), a gene which is regulation of cell volume; membrane potential stabilization, signal transduction and transepithelial transport. Accordingly, utilities of VGAM1538 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCN4. The function of CLCN4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM558. Hydroxyprostaglandin Dehydrogenase 15-(NAD) (HPGD, Accession NM\_000860) is another VGAM1538 host target gene. HPGD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPGD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPGD BINDING SITE, designated SEQ ID:6522, to the nucleotide sequence of VGAM1538 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4249.

[52833] Another function of VGAM1538 is therefore inhibition of Hydroxyprostaglandin Dehydrogenase 15-(NAD) (HPGD, Accession NM\_000860), a gene which converts cortisol to cortisone. Accordingly, utilities of VGAM1538 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPGD. The function of HPGD has been established by previous studies. Prostaglandins are involved in many physiologic and cellular processes, such as inflammation. Pichaud et al. (1997) noted that the NAD(+)-dependent 15-hydroxyprostaglandin dehydrogenase (15-PGDH, type I) is the main enzyme of prostaglandin degradation. By catalyzing the conversion of the 15-hydroxyl group of prostaglandins into a keto group, this ubiquitous enzyme strongly reduces the biologic activity of these molecules. The nucleotide sequence coding for PGDH1 was established by Ensor et al. (1990) who found a 801-bp open reading frame coding for a protein with 266 amino acids identical to the amino acid sequence established by Krook et al. (1990). Cortisol reduces the activity of PGDH in human placental cells. 11-beta hydroxysteroid dehydrogenase type II (HSD11B2; 218030) converts cortisol to cortisone. Schoof et al.

(2001) investigated a possible correlation between HSD11B2 and PGDH gene expression in the placenta of patients with preeclampsia. They concluded that, in preeclampsia, HSD11B2 mRNA expression is reduced, leading to a decrease of HSD11B2 activity. Furthermore, by means of an autocrine or paracrine mechanism, the diminished conversion of placental cortisol may lead to reduced PGDH mRNA expression. Animal model experiments lend further support to the function of HPGD. Coggins et al. (2002) generated mice deficient in *Pgdh* by targeted disruption. The *Pgdh*  $-/-$  pups died between 12 and 48 hours of life because of patent ductus arteriosus leading to congestive heart failure. Treatment with indomethacin rescued the phenotype. Coggins et al. (2002) concluded that alterations in PGE<sub>2</sub> metabolism by PGDH during the perinatal period is essential for the permanent closure of the ductus arteriosus.

[52834] It is appreciated that the abovementioned animal model for HPGD is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[52835] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

[52836] Schoof, E.; Girstl, M.; Frobenius, W.; Kirschbaum, M.; Dorr, H. G.; Rascher, W.; Dotsch, J. : Decreased gene expression of 11-beta-hydroxysteroid dehydrogenase type 2 and 15-hydroxyprostaglandin dehydrogenase in human placenta of patients with preeclampsia. J. Clin. Endocr. Metab. 86: 1313-1317, 2001. ; and

[52837] Pichaud, F.; Delage-Mourroux, R.; Pidoux, E.; Jullienne, A.; Rousseau-Merck, M.-F. : Chromosomal localization of the type-I 15-PGDH gene to 4q34-q35. Hum. Genet. 99: 279-281, 1997.

[52838] Further studies establishing the function and utilities of HPGD are found in John Hopkins OMIM database record ID 601688, and in cited publications numbered 6229-623 and 2793 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Timeless Homolog (Drosophila) (TIMELESS, Accession NM\_003920) is another VGAM1538 host target gene. TIMELESS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIMELESS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

TIMELESS BINDING SITE, designated SEQ ID:10006, to the nucleotide sequence of VGAM1538 RNA, herein designated VGAM RNA, also designated SEQ ID:4249.

[52839] Another function of VGAM1538 is therefore inhibition of Timeless Homolog (Drosophila) (TIMELESS, Accession NM\_003920), a gene which involves in circadian oscillation autoregulation. Accordingly, utilities of VGAM1538 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIMELESS. The function of TIMELESS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM409. Toll-like Receptor 5 (TLR5, Accession XM\_086576) is another VGAM1538 host target gene. TLR5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TLR5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLR5 BINDING SITE, designated SEQ ID:38774, to the nucleotide sequence of VGAM1538 RNA, herein designated VGAM RNA, also designated SEQ ID:4249.

[52840] Another function of VGAM1538 is therefore inhibition of

Toll-like Receptor 5 (TLR5, Accession XM\_086576), a gene which participates in the innate immune response to bacterial flagellins. Accordingly, utilities of VGAM1538 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLR5. The function of TLR5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM1126.KIAA1557 (Accession XM\_028289) is another VGAM1538 host target gene. KIAA1557 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1557 BINDING SITE, designated SEQ ID:30641, to the nucleotide sequence of VGAM1538 RNA, herein designated VGAM RNA, also designated SEQ ID:4249.

[52841] Another function of VGAM1538 is therefore inhibition of KIAA1557 (Accession XM\_028289). Accordingly, utilities of VGAM1538 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1557. Pleckstrin Homology Domain Containing, Fam-

ily A (phosphoinositide binding specific) Member 3 (PLEKHA3, Accession NM\_019091) is another VGAM1538 host target gene. PLEKHA3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PLEKHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLEKHA3 BINDING SITE, designated SEQ ID:21167, to the nucleotide sequence of VGAM1538 RNA, herein designated VGAM RNA, also designated SEQ ID:4249.

[52842] Another function of VGAM1538 is therefore inhibition of Pleckstrin Homology Domain Containing, Family A (phosphoinositide binding specific) Member 3 (PLEKHA3, Accession NM\_019091). Accordingly, utilities of VGAM1538 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLEKHA3. LOC133022 (Accession XM\_068144) is another VGAM1538 host target gene. LOC133022 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC133022, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the



complementarity of the nucleotide sequences of LOC133022 BINDING SITE, designated SEQ ID:37375, to the nucleotide sequence of VGAM1538 RNA, herein designated VGAM RNA, also designated SEQ ID:4249.

[52843] Another function of VGAM1538 is therefore inhibition of LOC133022 (Accession XM\_068144). Accordingly, utilities of VGAM1538 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133022. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1539 (VGAM1539) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52844] VGAM1539 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1539 was detected is described hereinabove with reference to Figs. 1–8.

[52845] VGAM1539 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1539 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[52846] VGAM1539 gene encodes a VGAM1539 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1539 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1539 precursor RNA is designated SEQ ID:1525, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1525 is located at position 60492 relative to the genome of Monkeypox Virus.

[52847] VGAM1539 precursor RNA folds onto itself, forming VGAM1539 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52848] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1539 folded precursor RNA into VGAM1539 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1539 RNA is designated SEQ ID:4250, and is provided hereinbelow with reference to the sequence listing part.

[52849] VGAM1539 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1539 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1539 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52850] VGAM1539 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1539 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1539 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1539 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1539 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52851] The complementary binding of VGAM1539 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1539 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1539 host target RNA into VGAM1539 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52852] It is appreciated that VGAM1539 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1539 host target genes. The mRNA of each one of this plurality of VGAM1539 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1539 RNA, herein designated VGAM RNA, and which when bound by VGAM1539 RNA causes inhibition of translation of respective one or more VGAM1539 host target proteins.

[52853] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1539 gene, herein designated VGAM GENE, on one or more VGAM1539 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52854] It is yet further appreciated that a function of VGAM1539 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1539 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1539 correlate with, and may be deduced from, the identity of the host target genes which VGAM1539 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52855] Nucleotide sequences of the VGAM1539 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1539 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1539 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1539 are further described hereinbelow with reference to Table 1.

[52856] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1539 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1539 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52857] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1539 gene, herein designated VGAM is inhibition of expression of VGAM1539 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1539 correlate with, and may be deduced from, the identity of the target genes which VGAM1539 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52858] Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542) is a VGAM1539 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45216, to the nucleotide sequence of VGAM1539 RNA, herein designated VGAM RNA, also designated SEQ ID:4250.

[52859] A function of VGAM1539 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM1539 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. Chromosome 20 Open Reading Frame 43 (C20orf43, Accession XM\_009549) is another VGAM1539 host target gene. C20orf43 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf43, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf43 BINDING SITE, designated SEQ ID:30113, to the nucleotide sequence of VGAM1539 RNA, herein designated VGAM RNA, also designated SEQ ID:4250.

[52860] Another function of VGAM1539 is therefore inhibition of Chromosome 20 Open Reading Frame 43 (C20orf43, Ac-



cession XM\_009549). Accordingly, utilities of VGAM1539 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf43.

KIAA1559 (Accession XM\_054472) is another VGAM1539 host target gene. KIAA1559 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1559 BINDING SITE, designated SEQ ID:36160, to the nucleotide sequence of VGAM1539 RNA, herein designated VGAM RNA, also designated SEQ ID:4250.

[52861] Another function of VGAM1539 is therefore inhibition of KIAA1559 (Accession XM\_054472). Accordingly, utilities of VGAM1539 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1559. LOC152179 (Accession XM\_098170) is another VGAM1539 host target gene. LOC152179 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC152179 BINDING SITE, designated SEQ ID:41431, to the nucleotide sequence of VGAM1539 RNA, herein designated VGAM RNA, also designated SEQ ID:4250.

[52862] Another function of VGAM1539 is therefore inhibition of LOC152179 (Accession XM\_098170). Accordingly, utilities of VGAM1539 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152179. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1540 (VGAM1540) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52863] VGAM1540 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1540 was detected is described hereinabove with reference to Figs. 1–8.

[52864] VGAM1540 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1540 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[52865] VGAM1540 gene encodes a VGAM1540 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1540 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1540 precursor RNA is designated SEQ ID:1526, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1526 is located at position 61618 relative to the genome of Monkeypox Virus.

[52866] VGAM1540 precursor RNA folds onto itself, forming VGAM1540 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52867] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1540 folded precursor RNA into VGAM1540 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1540 RNA is designated SEQ ID:4251, and is provided hereinbelow with reference to the sequence listing part.

[52868] VGAM1540 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1540 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1540 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52869] VGAM1540 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1540 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1540 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1540 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1540 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52870] The complementary binding of VGAM1540 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1540 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1540 host target RNA into VGAM1540 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52871] It is appreciated that VGAM1540 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1540 host target genes. The mRNA of each one of this plurality of VGAM1540 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1540 RNA, herein designated VGAM RNA, and which when bound by VGAM1540 RNA causes inhibition of translation of respective one or more VGAM1540 host target proteins.

[52872] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1540 gene, herein designated VGAM GENE, on one or more VGAM1540 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52873] It is yet further appreciated that a function of VGAM1540 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1540 correlate with, and may be deduced from, the identity of the host target genes which VGAM1540 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52874] Nucleotide sequences of the VGAM1540 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1540 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1540 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1540 are further described hereinbelow with reference to Table 1.

[52875] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1540 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1540 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52876] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1540 gene, herein designated VGAM is inhibition of expression of VGAM1540 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1540 correlate with, and may be deduced from, the identity of the target genes which VGAM1540 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52877] Apical Protein-like (*Xenopus laevis*) (APXL, Accession NM\_001649) is a VGAM1540 host target gene. APXL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APXL BINDING SITE, designated SEQ ID:7352, to the nucleotide sequence of VGAM1540 RNA, herein designated VGAM RNA, also designated SEQ ID:4251.



[52878] A function of VGAM1540 is therefore inhibition of Apical Protein-like (*Xenopus laevis*) (APXL, Accession NM\_001649), a gene which is implicated in amiloride-sensitive sodium channel activity. Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APXL. The function of APXL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Cockayne Syndrome 1 (classical) (CKN1, Accession NM\_000082) is another VGAM1540 host target gene. CKN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKN1 BINDING SITE, designated SEQ ID:5529, to the nucleotide sequence of VGAM1540 RNA, herein designated VGAM RNA, also designated SEQ ID:4251.

[52879] Another function of VGAM1540 is therefore inhibition of Cockayne Syndrome 1 (classical) (CKN1, Accession NM\_000082). Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with CKN1. High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483) is another VGAM1540 host target gene. HMGA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGA2 BINDING SITE, designated SEQ ID:9561, to the nucleotide sequence of VGAM1540 RNA, herein designated VGAM RNA, also designated SEQ ID:4251.

[52880] Another function of VGAM1540 is therefore inhibition of High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483), a gene which may affect transcription and cell differentiation; shares common DNA-binding motif with other HMG HMG I/Y family members. Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGA2. The function of HMGA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Zinc Finger Protein 36 (KOX 18) (ZNF36, Accession XM\_168302) is another VGAM1540

host target gene. ZNF36 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF36 BINDING SITE, designated SEQ ID:45101, to the nucleotide sequence of VGAM1540 RNA, herein designated VGAM RNA, also designated SEQ ID:4251.

[52881] Another function of VGAM1540 is therefore inhibition of Zinc Finger Protein 36 (KOX 18) (ZNF36, Accession XM\_168302), a gene which may be involved in transcriptional regulation. Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF36. The function of ZNF36 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM804.FLJ23191 (Accession NM\_024574) is another VGAM1540 host target gene. FLJ23191 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23191 BINDING SITE, designated SEQ ID:23803, to the nucleotide sequence of VGAM1540 RNA, herein designated VGAM RNA, also designated SEQ ID:4251.

[52882] Another function of VGAM1540 is therefore inhibition of FLJ23191 (Accession NM\_024574). Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23191. KIAA0841 (Accession XM\_049237) is another VGAM1540 host target gene. KIAA0841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0841 BINDING SITE, designated SEQ ID:35359, to the nucleotide sequence of VGAM1540 RNA, herein designated VGAM RNA, also designated SEQ ID:4251.

[52883] Another function of VGAM1540 is therefore inhibition of KIAA0841 (Accession XM\_049237). Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0841. Ring Finger Protein 20 (RNF20, Accession NM\_019592) is another VGAM1540 host target gene. RNF20 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RNF20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF20 BINDING SITE, designated SEQ ID:21213, to the nucleotide sequence of VGAM1540 RNA, herein designated VGAM RNA, also designated SEQ ID:4251.

[52884] Another function of VGAM1540 is therefore inhibition of Ring Finger Protein 20 (RNF20, Accession NM\_019592). Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF20. LOC118851 (Accession XM\_061180) is another VGAM1540 host target gene. LOC118851 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC118851, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118851 BINDING SITE, desig-

nated SEQ ID:37199, to the nucleotide sequence of VGAM1540 RNA, herein designated VGAM RNA, also designated SEQ ID:4251.

[52885] Another function of VGAM1540 is therefore inhibition of LOC118851 (Accession XM\_061180). Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118851. LOC150005 (Accession XM\_097795) is another VGAM1540 host target gene. LOC150005 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150005, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150005 BINDING SITE, designated SEQ ID:41122, to the nucleotide sequence of VGAM1540 RNA, herein designated VGAM RNA, also designated SEQ ID:4251.

[52886] Another function of VGAM1540 is therefore inhibition of LOC150005 (Accession XM\_097795). Accordingly, utilities of VGAM1540 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150005. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1541 (VGAM1541) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52887] VGAM1541 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1541 was detected is described hereinabove with reference to Figs. 1–8.

[52888] VGAM1541 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1541 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52889] VGAM1541 gene encodes a VGAM1541 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1541 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1541 precursor RNA is designated SEQ ID:1527, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1527 is located at position 63264 relative to the

genome of Monkeypox Virus.

[52890] VGAM1541 precursor RNA folds onto itself, forming VGAM1541 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52891] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1541 folded precursor RNA into VGAM1541 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1541 RNA is designated SEQ ID:4252, and is provided hereinbelow with reference to the sequence listing part.

[52892] VGAM1541 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1541 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1541 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52893] VGAM1541 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1541 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1541 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1541 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1541 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[52894] The complementary binding of VGAM1541 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1541 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1541 host target RNA into VGAM1541 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52895] It is appreciated that VGAM1541 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1541 host target genes. The mRNA of each one of this plurality of VGAM1541 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1541 RNA, herein designated VGAM RNA, and which when bound by VGAM1541 RNA causes inhibition of translation of respective one or more VGAM1541 host target proteins.

[52896] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1541 gene, herein designated VGAM GENE, on one or more VGAM1541 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52897] It is yet further appreciated that a function of VGAM1541 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1541 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1541 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52898] Nucleotide sequences of the VGAM1541 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1541 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1541 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1541 are further described hereinbelow with reference to Table 1.

[52899] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1541 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1541 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52900] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1541 gene, herein designated VGAM is inhibition of expression of VGAM1541 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1541 correlate with, and may be deduced

from, the identity of the target genes which VGAM1541 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52901] ATP-binding Cassette, Sub-family B (MDR/TAP), Member 10 (ABCB10, Accession NM\_012089) is a VGAM1541 host target gene. ABCB10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCB10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCB10 BINDING SITE, designated SEQ ID:14374, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52902] A function of VGAM1541 is therefore inhibition of ATP-binding Cassette, Sub-family B (MDR/TAP), Member 10 (ABCB10, Accession NM\_012089), a gene which a member of the superfamily of ATP-binding cassette (ABC) transporters. Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCB10. The function of ABCB10 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM1523. Adducin 1 (alpha) (ADD1, Accession NM\_014190) is another VGAM1541 host target gene. ADD1 BINDING SITE1 and ADD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADD1 BINDING SITE1 and ADD1 BINDING SITE2, designated SEQ ID:15474 and SEQ ID:15470 respectively, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52903] Another function of VGAM1541 is therefore inhibition of Adducin 1 (alpha) (ADD1, Accession NM\_014190), a gene which membrane-cytoskeleton- protein that promotes the assembly of the spectrin-actin network. Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADD1. The function of ADD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM474. Chemokine (C-C motif) Receptor 9

(CCR9, Accession NM\_006641) is another VGAM1541 host target gene. CCR9 BINDING SITE1 and CCR9 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCR9, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR9 BINDING SITE1 and CCR9 BINDING SITE2, designated SEQ ID:13432 and SEQ ID:22412 respectively, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52904] Another function of VGAM1541 is therefore inhibition of Chemokine (C-C motif) Receptor 9 (CCR9, Accession NM\_006641), a gene which binds beta-chemokine family and subsequently transduces a signal by increasing the intracellular calcium ions level. Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR9. The function of CCR9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1324.CGTHBA (Accession NM\_012075) is another VGAM1541 host target gene. CGTHBA BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CGTHBA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGTHBA BINDING SITE, designated SEQ ID:14364, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52905] Another function of VGAM1541 is therefore inhibition of CGTHBA (Accession NM\_012075). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGTHBA. Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM\_114147) is another VGAM1541 host target gene. EIF1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF1A BINDING SITE, designated SEQ ID:42721, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.



[52906] Another function of VGAM1541 is therefore inhibition of Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM\_114147), a gene which seems to be required for maximal rate of protein biosynthesis. Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF1A. The function of EIF1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440) is another VGAM1541 host target gene. EXTL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EXTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL3 BINDING SITE, designated SEQ ID:7171, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52907] Another function of VGAM1541 is therefore inhibition of Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440), a gene which is a member of the multiple ex-

ostoses gene family. Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL3. The function of EXTL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Growth Hormone Receptor (GHR, Accession NM\_000163) is another VGAM1541 host target gene. GHR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GHR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GHR BINDING SITE, designated SEQ ID:5671, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52908] Another function of VGAM1541 is therefore inhibition of Growth Hormone Receptor (GHR, Accession NM\_000163). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GHR. Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262) is another VGAM1541 host target gene. HS2ST1 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HS2ST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS2ST1 BINDING SITE, designated SEQ ID:14576, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52909] Another function of VGAM1541 is therefore inhibition of Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS2ST1. Nucleobindin 1 (NUCB1, Accession NM\_006184) is another VGAM1541 host target gene. NUCB1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NUCB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUCB1 BINDING SITE, designated SEQ ID:12851, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52910] Another function of VGAM1541 is therefore inhibition of Nucleobindin 1 (NUCB1, Accession NM\_006184), a gene which may have a role in calcium homeostasis. Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUCB1. The function of NUCB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1523. CDC42 Binding Protein Kinase Beta (DMPK-like) (CDC42BPB, Accession NM\_006035) is another VGAM1541 host target gene. CDC42BPB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC42BPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC42BPB BINDING SITE, designated SEQ ID:12658, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52911] Another function of VGAM1541 is therefore inhibition of CDC42 Binding Protein Kinase Beta (DMPK-like) (CDC42BPB, Accession NM\_006035). Accordingly, utilities

of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC42BPB. DKFZP566B183 (Accession NM\_015509) is another VGAM1541 host target gene. DKFZP566B183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566B183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566B183 BINDING SITE, designated SEQ ID:17769, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52912] Another function of VGAM1541 is therefore inhibition of DKFZP566B183 (Accession NM\_015509). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566B183. DKFZP566I1024 (Accession XM\_046506) is another VGAM1541 host target gene. DKFZP566I1024 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566I1024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566I1024 BINDING SITE, designated SEQ ID:34735, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52913] Another function of VGAM1541 is therefore inhibition of DKFZP566I1024 (Accession XM\_046506). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566I1024. DKFZp761B0514 (Accession NM\_032289) is another VGAM1541 host target gene. DKFZp761B0514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761B0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761B0514 BINDING SITE, designated SEQ ID:26053, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52914] Another function of VGAM1541 is therefore inhibition of DKFZp761B0514 (Accession NM\_032289). Accordingly, utilities of VGAM1541 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZp761B0514. FLJ13305 (Accession XM\_117270) is another VGAM1541 host target gene. FLJ13305 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13305 BINDING SITE, designated SEQ ID:43345, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52915] Another function of VGAM1541 is therefore inhibition of FLJ13305 (Accession XM\_117270). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13305. KIAA0265 (Accession XM\_045954) is another VGAM1541 host target gene. KIAA0265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0265 BINDING SITE, designated SEQ ID:34620, to the

nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52916] Another function of VGAM1541 is therefore inhibition of KIAA0265 (Accession XM\_045954). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0265. KIAA1117 (Accession XM\_028219) is another VGAM1541 host target gene. KIAA1117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1117 BINDING SITE, designated SEQ ID:30632, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52917] Another function of VGAM1541 is therefore inhibition of KIAA1117 (Accession XM\_028219). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1117. KIAA1319 (Accession NM\_020770) is another VGAM1541 host target gene. KIAA1319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by KIAA1319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1319 BINDING SITE, designated SEQ ID:21870, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52918] Another function of VGAM1541 is therefore inhibition of KIAA1319 (Accession NM\_020770). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1319. Nudix (nucleoside diphosphate linked moiety X)-type Motif 13 (NUDT13, Accession XM\_032512) is another VGAM1541 host target gene. NUDT13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUDT13 BINDING SITE, designated SEQ ID:31664, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52919] Another function of VGAM1541 is therefore inhibition of

Nudix (nucleoside diphosphate linked moiety X)-type Motif 13 (NUDT13, Accession XM\_032512). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUDT13. SSH2 (Accession XM\_030846) is another VGAM1541 host target gene. SSH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSH2 BINDING SITE, designated SEQ ID:31176, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52920] Another function of VGAM1541 is therefore inhibition of SSH2 (Accession XM\_030846). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH2. Signal Sequence Receptor, Alpha (translocon-associated protein alpha) (SSR1, Accession NM\_003144) is another VGAM1541 host target gene. SSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSR1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSR1 BINDING SITE, designated SEQ ID:9113, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52921] Another function of VGAM1541 is therefore inhibition of Signal Sequence Receptor, Alpha (translocon-associated protein alpha) (SSR1, Accession NM\_003144). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSR1. TAF9-like RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 31kDa (TAF9L, Accession NM\_015975) is another VGAM1541 host target gene. TAF9L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAF9L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF9L BINDING SITE, designated SEQ ID:18072, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52922] Another function of VGAM1541 is therefore inhibition of TAF9-like RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 31kDa (TAF9L, Accession NM\_015975). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF9L. LOC115294 (Accession XM\_054302) is another VGAM1541 host target gene. LOC115294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115294 BINDING SITE, designated SEQ ID:36145, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52923] Another function of VGAM1541 is therefore inhibition of LOC115294 (Accession XM\_054302). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115294. LOC150271 (Accession XM\_097859) is another VGAM1541 host target gene. LOC150271 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41166, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52924] Another function of VGAM1541 is therefore inhibition of LOC150271 (Accession XM\_097859). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC151877 (Accession XM\_098132) is another VGAM1541 host target gene. LOC151877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151877 BINDING SITE, designated SEQ ID:41398, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52925] Another function of VGAM1541 is therefore inhibition of LOC151877 (Accession XM\_098132). Accordingly, utilities

of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151877. LOC152300 (Accession XM\_087432) is another VGAM1541 host target gene. LOC152300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152300 BINDING SITE, designated SEQ ID:39248, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52926] Another function of VGAM1541 is therefore inhibition of LOC152300 (Accession XM\_087432). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152300. LOC154084 (Accession XM\_098468) is another VGAM1541 host target gene. LOC154084 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC154084 BINDING SITE, designated SEQ ID:41685, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52927] Another function of VGAM1541 is therefore inhibition of LOC154084 (Accession XM\_098468). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154084. LOC158402 (Accession XM\_098936) is another VGAM1541 host target gene. LOC158402 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158402, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158402 BINDING SITE, designated SEQ ID:41976, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52928] Another function of VGAM1541 is therefore inhibition of LOC158402 (Accession XM\_098936). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158402. LOC162333 (Accession XM\_102591) is another VGAM1541 host target gene. LOC162333 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42124, to the nucleotide sequence of VGAM1541 RNA, herein designated VGAM RNA, also designated SEQ ID:4252.

[52929] Another function of VGAM1541 is therefore inhibition of LOC162333 (Accession XM\_102591). Accordingly, utilities of VGAM1541 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1542 (VGAM1542) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52930] VGAM1542 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1542 was detected is described hereinabove with reference to Figs. 1-8.



[52931] VGAM1542 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus.

VGAM1542 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52932] VGAM1542 gene encodes a VGAM1542 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1542 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1542 precursor RNA is designated SEQ ID:1528, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1528 is located at position 56199 relative to the genome of Variola Virus.

[52933] VGAM1542 precursor RNA folds onto itself, forming VGAM1542 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[52934] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1542 folded precursor RNA into VGAM1542 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1542 RNA is designated SEQ ID:4253, and is provided hereinbelow with reference to the sequence listing part.

[52935] VGAM1542 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1542 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1542 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52936] VGAM1542 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1542 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1542 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1542 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1542 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52937] The complementary binding of VGAM1542 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1542 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1542 host target RNA into VGAM1542 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[52938] It is appreciated that VGAM1542 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1542 host target genes. The mRNA of each one of this plurality of VGAM1542 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1542 RNA, herein designated VGAM RNA, and which when bound by VGAM1542 RNA causes inhibition of translation of respective one or more VGAM1542 host target proteins.

[52939] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1542 gene, herein designated VGAM GENE, on one or more VGAM1542 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52940] It is yet further appreciated that a function of VGAM1542 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1542 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1542 correlate with, and may be deduced from, the identity of the host target genes which VGAM1542 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52941] Nucleotide sequences of the VGAM1542 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1542 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1542 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1542 are further described hereinbelow with reference to Table 1.

[52942] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1542 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1542 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52943] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1542 gene, herein designated VGAM is inhibition of expression of VGAM1542 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1542 correlate with, and may be deduced from, the identity of the target genes which VGAM1542 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52944] LOC147057 (Accession XM\_097166) is a VGAM1542 host target gene. LOC147057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LOC147057 BINDING SITE, designated SEQ ID:40782, to the nucleotide sequence of VGAM1542 RNA, herein designated VGAM RNA, also designated SEQ ID:4253.

[52945] A function of VGAM1542 is therefore inhibition of LOC147057 (Accession XM\_097166). Accordingly, utilities of VGAM1542 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147057. LOC154739 (Accession XM\_098602) is another VGAM1542 host target gene. LOC154739 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154739 BINDING SITE, designated SEQ ID:41716, to the nucleotide sequence of VGAM1542 RNA, herein designated VGAM RNA, also designated SEQ ID:4253.

[52946] Another function of VGAM1542 is therefore inhibition of LOC154739 (Accession XM\_098602). Accordingly, utilities of VGAM1542 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154739. LOC203276 (Accession XM\_117523) is an-

other VGAM1542 host target gene. LOC203276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203276 BINDING SITE, designated SEQ ID:43483, to the nucleotide sequence of VGAM1542 RNA, herein designated VGAM RNA, also designated SEQ ID:4253.

[52947] Another function of VGAM1542 is therefore inhibition of LOC203276 (Accession XM\_117523). Accordingly, utilities of VGAM1542 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203276. LOC203305 (Accession XM\_117529) is another VGAM1542 host target gene. LOC203305 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203305 BINDING SITE, designated SEQ ID:43507, to the nucleotide sequence of VGAM1542 RNA, herein designated VGAM RNA, also designated SEQ ID:4253.



[52948] Another function of VGAM1542 is therefore inhibition of LOC203305 (Accession XM\_117529). Accordingly, utilities of VGAM1542 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203305. LOC254243 (Accession XM\_173233) is another VGAM1542 host target gene. LOC254243 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254243 BINDING SITE, designated SEQ ID:46509, to the nucleotide sequence of VGAM1542 RNA, herein designated VGAM RNA, also designated SEQ ID:4253.

[52949] Another function of VGAM1542 is therefore inhibition of LOC254243 (Accession XM\_173233). Accordingly, utilities of VGAM1542 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254243. LOC90038 (Accession XM\_028305) is another VGAM1542 host target gene. LOC90038 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90038, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90038 BINDING SITE, designated SEQ ID:30646, to the nucleotide sequence of VGAM1542 RNA, herein designated VGAM RNA, also designated SEQ ID:4253.

[52950] Another function of VGAM1542 is therefore inhibition of LOC90038 (Accession XM\_028305). Accordingly, utilities of VGAM1542 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90038. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1543 (VGAM1543) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52951] VGAM1543 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1543 was detected is described hereinabove with reference to Figs. 1–8.

[52952] VGAM1543 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia Virus. VGAM1543 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[52953] VGAM1543 gene encodes a VGAM1543 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1543 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1543 precursor RNA is designated SEQ ID:1529, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1529 is located at position 66348 relative to the genome of Vaccinia Virus.

[52954] VGAM1543 precursor RNA folds onto itself, forming VGAM1543 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[52955] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1543 folded precursor RNA into VGAM1543

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1543 RNA is designated SEQ ID:4254, and is provided hereinbelow with reference to the sequence listing part.

[52956] VGAM1543 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1543 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1543 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[52957] VGAM1543 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1543 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1543 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1543 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1543 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[52958] The complementary binding of VGAM1543 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1543 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1543 host target RNA into VGAM1543 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[52959] It is appreciated that VGAM1543 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1543 host target genes. The mRNA of each one of this plurality of VGAM1543 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1543 RNA, herein designated VGAM RNA, and which when bound by VGAM1543 RNA causes inhibition of translation of respective one or more VGAM1543 host target proteins.

[52960] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1543 gene, herein designated VGAM GENE, on one or more VGAM1543 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[52961] It is yet further appreciated that a function of VGAM1543 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGAM1543 correlate with, and may be deduced from, the identity of the host target genes which VGAM1543 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[52962] Nucleotide sequences of the VGAM1543 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1543 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1543 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1543 are further described hereinbelow with reference to Table 1.

[52963] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1543 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1543 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[52964] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1543 gene, herein designated VGAM is inhibition of expression of VGAM1543 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1543 correlate with, and may be deduced from, the identity of the target genes which VGAM1543 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[52965] ATP-binding Cassette, Sub-family B (MDR/TAP), Member 10 (ABCB10, Accession NM\_012089) is a VGAM1543 host target gene. ABCB10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCB10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCB10 BINDING SITE, designated SEQ ID:14374, to the nucleotide sequence of



VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52966] A function of VGAM1543 is therefore inhibition of ATP-binding Cassette, Sub-family B (MDR/TAP), Member 10 (ABCB10, Accession NM\_012089), a gene which a member of the superfamily of ATP-binding cassette (ABC) transporters. Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCB10. The function of ABCB10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1523. Adducin 1 (alpha) (ADD1, Accession NM\_014189) is another VGAM1543 host target gene. ADD1 BINDING SITE1 and ADD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADD1 BINDING SITE1 and ADD1 BINDING SITE2, designated SEQ ID:15470 and SEQ ID:15474 respectively, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4254.

[52967] Another function of VGAM1543 is therefore inhibition of Adducin 1 (alpha) (ADD1, Accession NM\_014189), a gene which membrane-cytoskeleton- protein that promotes the assembly of the spectrin-actin network. Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADD1. The function of ADD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM474. Chemokine (C-C motif) Receptor 9 (CCR9, Accession NM\_031200) is another VGAM1543 host target gene. CCR9 BINDING SITE1 and CCR9 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCR9, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR9 BINDING SITE1 and CCR9 BINDING SITE2, designated SEQ ID:25249 and SEQ ID:22412 respectively, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52968] Another function of VGAM1543 is therefore inhibition of

Chemokine (C-C motif) Receptor 9 (CCR9, Accession NM\_031200), a gene which binds beta-chemokine family and subsequently transduces a signal by increasing the intracellular calcium ions level. Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR9. The function of CCR9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1324.CGTHBA (Accession NM\_012075) is another VGAM1543 host target gene. CGTHBA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGTHBA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGTHBA BINDING SITE, designated SEQ ID:14364, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52969] Another function of VGAM1543 is therefore inhibition of CGTHBA (Accession NM\_012075). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

CGTHBA. Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM\_114147) is another VGAM1543 host target gene. EIF1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF1A BINDING SITE, designated SEQ ID:42721, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52970] Another function of VGAM1543 is therefore inhibition of Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM\_114147), a gene which seems to be required for maximal rate of protein biosynthesis. Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF1A. The function of EIF1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440) is another VGAM1543 host target gene. EXTL3 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by EXTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL3 BINDING SITE, designated SEQ ID:7171, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52971] Another function of VGAM1543 is therefore inhibition of Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440), a gene which is a member of the multiple exostoses gene family. Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL3. The function of EXTL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Growth Hormone Receptor (GHR, Accession NM\_000163) is another VGAM1543 host target gene. GHR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GHR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of GHR BINDING SITE, designated SEQ ID:5671, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52972] Another function of VGAM1543 is therefore inhibition of Growth Hormone Receptor (GHR, Accession NM\_000163). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GHR. Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262) is another VGAM1543 host target gene. HS2ST1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HS2ST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS2ST1 BINDING SITE, designated SEQ ID:14576, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52973] Another function of VGAM1543 is therefore inhibition of Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with HS2ST1. Nucleobindin 1 (NUCB1, Accession NM\_006184) is another VGAM1543 host target gene. NUCB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUCB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUCB1 BINDING SITE, designated SEQ ID:12851, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52974] Another function of VGAM1543 is therefore inhibition of Nucleobindin 1 (NUCB1, Accession NM\_006184), a gene which may have a role in calcium homeostasis. Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUCB1. The function of NUCB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1523. CDC42 Binding Protein Kinase Beta (DMPK-like) (CDC42BPB, Accession NM\_006035) is another VGAM1543 host target gene. CDC42BPB BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by CDC42BPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC42BPB BINDING SITE, designated SEQ ID:12658, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52975] Another function of VGAM1543 is therefore inhibition of CDC42 Binding Protein Kinase Beta (DMPK-like) (CDC42BPB, Accession NM\_006035). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC42BPB. DKFZP566B183 (Accession NM\_015509) is another VGAM1543 host target gene. DKFZP566B183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566B183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566B183 BINDING SITE, designated SEQ ID:17769, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ



ID:4254.

[52976] Another function of VGAM1543 is therefore inhibition of DKFZP566B183 (Accession NM\_015509). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566B183. DKFZP566I1024 (Accession XM\_046506) is another VGAM1543 host target gene. DKFZP566I1024 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566I1024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566I1024 BINDING SITE, designated SEQ ID:34735, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52977] Another function of VGAM1543 is therefore inhibition of DKFZP566I1024 (Accession XM\_046506). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566I1024. DKFZp761B0514 (Accession NM\_032289) is another VGAM1543 host target gene. DKFZp761B0514 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by DKFZp761B0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761B0514 BINDING SITE, designated SEQ ID:26053, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52978] Another function of VGAM1543 is therefore inhibition of DKFZp761B0514 (Accession NM\_032289). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761B0514. FLJ13305 (Accession XM\_117270) is another VGAM1543 host target gene. FLJ13305 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13305 BINDING SITE, designated SEQ ID:43345, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52979] Another function of VGAM1543 is therefore inhibition of

FLJ13305 (Accession XM\_117270). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13305. KIAA0265 (Accession XM\_045954) is another VGAM1543 host target gene. KIAA0265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0265 BINDING SITE, designated SEQ ID:34620, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52980] Another function of VGAM1543 is therefore inhibition of KIAA0265 (Accession XM\_045954). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0265. KIAA1117 (Accession XM\_028219) is another VGAM1543 host target gene. KIAA1117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1117 BINDING SITE, designated SEQ ID:30632, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52981] Another function of VGAM1543 is therefore inhibition of KIAA1117 (Accession XM\_028219). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1117. KIAA1319 (Accession NM\_020770) is another VGAM1543 host target gene. KIAA1319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1319 BINDING SITE, designated SEQ ID:21870, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52982] Another function of VGAM1543 is therefore inhibition of KIAA1319 (Accession NM\_020770). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1319. Nudix (nucleoside diphosphate linked moiety

X)-type Motif 13 (NUDT13, Accession XM\_032512) is another VGAM1543 host target gene. NUDT13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUDT13 BINDING SITE, designated SEQ ID:31664, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52983] Another function of VGAM1543 is therefore inhibition of Nudix (nucleoside diphosphate linked moiety X)-type Motif 13 (NUDT13, Accession XM\_032512). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUDT13. SSH2 (Accession XM\_030846) is another VGAM1543 host target gene. SSH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSH2 BINDING SITE, designated SEQ ID:31176, to the nucleotide sequence of

VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52984] Another function of VGAM1543 is therefore inhibition of SSH2 (Accession XM\_030846). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH2. Signal Sequence Receptor, Alpha (translocon-associated protein alpha) (SSR1, Accession NM\_003144) is another VGAM1543 host target gene. SSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSR1 BINDING SITE, designated SEQ ID:9113, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52985] Another function of VGAM1543 is therefore inhibition of Signal Sequence Receptor, Alpha (translocon-associated protein alpha) (SSR1, Accession NM\_003144). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSR1. TAF9-like RNA Polymerase II, TATA Box Bind-

ing Protein (TBP)–associated Factor, 31kDa (TAF9L, Accession NM\_015975) is another VGAM1543 host target gene. TAF9L BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TAF9L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF9L BINDING SITE, designated SEQ ID:18072, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52986] Another function of VGAM1543 is therefore inhibition of TAF9–like RNA Polymerase II, TATA Box Binding Protein (TBP)–associated Factor, 31kDa (TAF9L, Accession NM\_015975). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF9L. LOC115294 (Accession XM\_054302) is another VGAM1543 host target gene. LOC115294 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC115294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu–

cleotide sequences of LOC115294 BINDING SITE, designated SEQ ID:36145, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52987] Another function of VGAM1543 is therefore inhibition of LOC115294 (Accession XM\_054302). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115294. LOC150271 (Accession XM\_097859) is another VGAM1543 host target gene. LOC150271 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41166, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52988] Another function of VGAM1543 is therefore inhibition of LOC150271 (Accession XM\_097859). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC151877 (Accession XM\_098132) is an-



other VGAM1543 host target gene. LOC151877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151877 BINDING SITE, designated SEQ ID:41398, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52989] Another function of VGAM1543 is therefore inhibition of LOC151877 (Accession XM\_098132). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151877. LOC152300 (Accession XM\_087432) is another VGAM1543 host target gene. LOC152300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152300 BINDING SITE, designated SEQ ID:39248, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52990] Another function of VGAM1543 is therefore inhibition of LOC152300 (Accession XM\_087432). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152300. LOC154084 (Accession XM\_098468) is another VGAM1543 host target gene. LOC154084 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154084 BINDING SITE, designated SEQ ID:41685, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52991] Another function of VGAM1543 is therefore inhibition of LOC154084 (Accession XM\_098468). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154084. LOC158402 (Accession XM\_098936) is another VGAM1543 host target gene. LOC158402 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158402, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158402 BINDING SITE, designated SEQ ID:41976, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52992] Another function of VGAM1543 is therefore inhibition of LOC158402 (Accession XM\_098936). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158402. LOC162333 (Accession XM\_102591) is another VGAM1543 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42124, to the nucleotide sequence of VGAM1543 RNA, herein designated VGAM RNA, also designated SEQ ID:4254.

[52993] Another function of VGAM1543 is therefore inhibition of LOC162333 (Accession XM\_102591). Accordingly, utilities of VGAM1543 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC162333. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1544 (VGAM1544) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[52994] VGAM1544 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1544 was detected is described hereinabove with reference to Figs. 1–8.

[52995] VGAM1544 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1544 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[52996] VGAM1544 gene encodes a VGAM1544 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1544 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1544 precursor RNA is designated SEQ ID:1530, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1530 is located at position 50463 relative to the genome of Variola Virus.

- [52997] VGAM1544 precursor RNA folds onto itself, forming VGAM1544 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [52998] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1544 folded precursor RNA into VGAM1544 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1544 RNA is designated SEQ ID:4255, and is provided hereinbelow with reference to the sequence listing part.

[52999] VGAM1544 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1544 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1544 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53000] VGAM1544 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1544 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1544 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1544 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1544 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53001] The complementary binding of VGAM1544 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1544 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1544 host target RNA into VGAM1544 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53002] It is appreciated that VGAM1544 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1544 host target genes. The mRNA of each one of this plurality of VGAM1544 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1544 RNA, herein designated VGAM RNA, and which when bound by VGAM1544 RNA causes

inhibition of translation of respective one or more VGAM1544 host target proteins.

[53003] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1544 gene, herein designated VGAM GENE, on one or more VGAM1544 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).



[53004] It is yet further appreciated that a function of VGAM1544 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1544 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1544 correlate with, and may be deduced from, the identity of the host target genes which VGAM1544 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53005] Nucleotide sequences of the VGAM1544 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1544 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1544 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1544 are further described hereinbelow with reference to Table 1.

[53006] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1544 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1544 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[53007] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1544 gene, herein designated VGAM is inhibition of expression of VGAM1544 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1544 correlate with, and may be deduced from, the identity of the target genes which VGAM1544 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53008] ATP-binding Cassette, Sub-family A (ABC1), Member 3 (ABCA3, Accession NM\_001089) is a VGAM1544 host target gene. ABCA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCA3 BINDING SITE, designated SEQ ID:6743, to the nucleotide sequence of VGAM1544 RNA, herein designated VGAM RNA, also designated SEQ ID:4255.

[53009] A function of VGAM1544 is therefore inhibition of ATP-binding Cassette, Sub-family A (ABC1), Member 3 (ABCA3, Accession NM\_001089), a gene which may be a trans-

porter, may act as an efflux pump for chemotherapeutics drugs. Accordingly, utilities of VGAM1544 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCA3. The function of ABCA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM336. Cathepsin B (CTSB, Accession XM\_035662) is another VGAM1544 host target gene. CTSB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTSB BINDING SITE, designated SEQ ID:32328, to the nucleotide sequence of VGAM1544 RNA, herein designated VGAM RNA, also designated SEQ ID:4255.

[53010] Another function of VGAM1544 is therefore inhibition of Cathepsin B (CTSB, Accession XM\_035662). Accordingly, utilities of VGAM1544 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTSB. Oxytocin Receptor (OXTR, Accession NM\_000916) is another VGAM1544 host target gene.

OXTR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OXTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OXTR BINDING SITE, designated SEQ ID:6622, to the nucleotide sequence of VGAM1544 RNA, herein designated VGAM RNA, also designated SEQ ID:4255.

[53011] Another function of VGAM1544 is therefore inhibition of Oxytocin Receptor (OXTR, Accession NM\_000916), a gene which induces inward ion currents. Accordingly, utilities of VGAM1544 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OXTR. The function of OXTR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM636. Protein Kinase, AMP-activated, Alpha 2 Catalytic Subunit (PRKAA2, Accession NM\_006252) is another VGAM1544 host target gene. PRKAA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKAA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of PRKAA2 BINDING SITE, designated SEQ ID:12928, to the nucleotide sequence of VGAM1544 RNA, herein designated VGAM RNA, also designated SEQ ID:4255.

[53012] Another function of VGAM1544 is therefore inhibition of Protein Kinase, AMP-activated, Alpha 2 Catalytic Subunit (PRKAA2, Accession NM\_006252), a gene which are responsible for the regulation of fatty acid synthesis by phosphorylation of acetyl-coa carboxylase. Accordingly, utilities of VGAM1544 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAA2. The function of PRKAA2 has been established by previous studies. AMP-activated protein kinase plays a key role in the regulation of fatty acid and cholesterol metabolism (Hardie, 1992; Hardie and MacKintosh, 1992). In vitro, it phosphorylates and inactivates 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR; 142910) and acetyl-CoA carboxylase (ACC; 200350), key enzymes involved in regulating de novo biosynthesis of cholesterol and fatty acids, respectively. See PRKAA1 (OMIM Ref. No. 602739) for additional background. Beri et al. (1994) used a cDNA encoding rat liver AMPK to isolate human skeletal muscle AMPK cDNA clones. The human

cDNA was more than 90% homologous to the rat sequence and predicted a protein of 62.3 kD that closely agreed with the mass of human AMPK observed in Western blots of human tissue extracts. A cDNA probe was used to identify a 9.5-kb transcript in several human tissues and to isolate human genomic clones. Stapleton et al. (1997) showed that rat liver Ampk-alpha-2 is associated with Ampk-beta-1 (PRKAB1; 602740) and Ampk-gamma-1 (PRKAG1; 602742). They noted that Ampk-alpha-1 (OMIM Ref. No. PRKAA1) is also associated with these beta and gamma isoforms. Beri et al. (1994) used PCR mapping of rodent/human hybrid cell lines to localize the human AMPK gene to chromosome 1, and they sublocalized the AMPK gene to 1p31 by fluorescence in situ hybridization with a human genomic clone. (The cDNA referred to as AMPK by Beri et al. (1994) encodes the alpha-2 subunit of AMPK.) Tsujikawa et al. (1998) determined that PRKAA2 and the CDC-like kinase-2 gene (CLK2; 602989) are located in the same interval of approximately 2.6 cM between D1S2890 and D1S2801. They suggested that CLK2 and PRKAA2 are possible candidate genes for gelatinous drop-like corneal dystrophy (OMIM Ref. No. 204870). Mu et al. (2001) investigated the role of the metabolic sensor

AMPK in the regulation of glucose transport in skeletal muscle. Expression in mouse muscle of a dominant inhibitory mutant of Ampk- $\alpha$ -2 completely blocked the ability of hypoxia and 5-aminoimidazole-4-carboxamide ribonucleoside (AICAR) to activate hexose uptake, while only partially reducing contraction-stimulated hexose uptake. These data indicated that AMPK transmits a portion of the signal by which muscle contraction increases glucose uptake, but other AMPK-independent pathways also contribute to the response. Minokoshi et al. (2002) demonstrated that leptin (OMIM Ref. No. 164160) selectively stimulates phosphorylation and activation of AMPK- $\alpha$ -2 in skeletal muscle, thus establishing an additional signaling pathway for leptin. Early activation of AMPK occurs by leptin acting directly on muscle, whereas later activation depends on leptin functioning through the hypothalamic-sympathetic nervous system axis. In parallel with its activation of AMPK, leptin suppresses the activity of ACC (200350, 601557), thereby stimulating the oxidation of fatty acids in muscle. Blocking AMPK activation inhibits the phosphorylation of ACC stimulated by leptin. Minokoshi et al. (2002) concluded that their data identify AMPK as a principal mediator of the effects of leptin on

fatty acid metabolism in muscle.

[53013] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53014] Minokoshi, Y.; Kim, Y.-B.; Peroni, O. D.; Fryer, L. G. D.; Muller, C.; Carling, D.; Kahn, B. B. : Leptin stimulates fatty-acid oxidation by activating AMP-activated protein kinase. Nature 415: 339-343, 2002. ; and

[53015] Mu, J.; Brozinick, J. T., Jr.; Valladares, O.; Bucan, M.; Birnbaum, M. J. : A role for AMP-activated protein kinase in contraction- and hypoxia-regulated glucose transport in skeletal m.

[53016] Further studies establishing the function and utilities of PRKAA2 are found in John Hopkins OMIM database record ID 600497, and in cited publications numbered 10692-10694, 10329, 10695-1069 and 1355 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0970 (Accession NM\_014923) is another VGAM1544 host target gene. KIAA0970 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.



Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0970 BINDING SITE, designated SEQ ID:17202, to the nucleotide sequence of VGAM1544 RNA, herein designated VGAM RNA, also designated SEQ ID:4255.

[53017] Another function of VGAM1544 is therefore inhibition of KIAA0970 (Accession NM\_014923). Accordingly, utilities of VGAM1544 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0970. LOC91694 (Accession XM\_040082) is another VGAM1544 host target gene. LOC91694 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91694 BINDING SITE, designated SEQ ID:33249, to the nucleotide sequence of VGAM1544 RNA, herein designated VGAM RNA, also designated SEQ ID:4255.

[53018] Another function of VGAM1544 is therefore inhibition of LOC91694 (Accession XM\_040082). Accordingly, utilities of VGAM1544 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC91694. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1545 (VGAM1545) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53019] VGAM1545 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1545 was detected is described hereinabove with reference to Figs. 1–8.

[53020] VGAM1545 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1545 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53021] VGAM1545 gene encodes a VGAM1545 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1545 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1545 precursor RNA is designated SEQ ID:1531, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1531 is located at position 53558 relative to the genome of Variola Virus.

- [53022] VGAM1545 precursor RNA folds onto itself, forming VGAM1545 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [53023] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1545 folded precursor RNA into VGAM1545 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1545 RNA is designated SEQ ID:4256, and is provided hereinbelow with reference to the sequence listing part.

[53024] VGAM1545 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1545 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1545 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53025] VGAM1545 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1545 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1545 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1545 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1545 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[53026] The complementary binding of VGAM1545 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1545 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1545 host target RNA into VGAM1545 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53027] It is appreciated that VGAM1545 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1545 host target genes. The mRNA of each one of this plurality of VGAM1545 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1545 RNA, herein designated VGAM RNA, and which when bound by VGAM1545 RNA causes

inhibition of translation of respective one or more VGAM1545 host target proteins.

[53028] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1545 gene, herein designated VGAM GENE, on one or more VGAM1545 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53029] It is yet further appreciated that a function of VGAM1545 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1545 include diagnosis, prevention and

treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1545 correlate with, and may be deduced from, the identity of the host target genes which VGAM1545 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53030] Nucleotide sequences of the VGAM1545 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1545 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1545 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1545 are further described hereinbelow with reference to Table 1.

[53031] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1545 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1545 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53032] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1545 gene, herein designated VGAM is inhibition of expression of VGAM1545 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1545 correlate with, and may be deduced from, the identity of the target genes which VGAM1545 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53033] C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252) is a VGAM1545 host target gene. CLECSF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLECSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF5 BINDING SITE, designated SEQ ID:14918, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53034] A function of VGAM1545 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252). Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF5. Early Growth Re-



sponse 3 (EGR3, Accession XM\_005040) is another VGAM1545 host target gene. EGR3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EGR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGR3 BINDING SITE, designated SEQ ID:29956, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53035] Another function of VGAM1545 is therefore inhibition of Early Growth Response 3 (EGR3, Accession XM\_005040), a gene which is a putative transcription factor. Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGR3. The function of EGR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM189. Fukuyama Type Congenital Muscular Dystrophy (fukutin) (FCMD, Accession NM\_006731) is another VGAM1545 host target gene. FCMD BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FCMD, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FCMD BINDING SITE, designated SEQ ID:13577, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53036] Another function of VGAM1545 is therefore inhibition of Fukuyama Type Congenital Muscular Dystrophy (fukutin) (FCMD, Accession NM\_006731). Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FCMD. Nuclear Receptor Subfamily 3, Group C, Member 1 (glucocorticoid receptor) (NR3C1, Accession NM\_000176) is another VGAM1545 host target gene. NR3C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NR3C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR3C1 BINDING SITE, designated SEQ ID:5686, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53037] Another function of VGAM1545 is therefore inhibition of

Nuclear Receptor Subfamily 3, Group C, Member 1 (glucocorticoid receptor) (NR3C1, Accession NM\_000176). Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR3C1. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily A, Member 3 (SMARCA3, Accession NM\_003071) is another VGAM1545 host target gene. SMARCA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMARCA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCA3 BINDING SITE, designated SEQ ID:9037, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53038] Another function of VGAM1545 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily A, Member 3 (SMARCA3, Accession NM\_003071), a gene which is involved in chromatin assembly and remodeling. Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with SMARCA3. The function of SMARCA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1330. Chromosome 12 Open Reading Frame 22 (C12orf22, Accession NM\_030809) is another VGAM1545 host target gene. C12orf22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C12orf22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C12orf22 BINDING SITE, designated SEQ ID:25125, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53039] Another function of VGAM1545 is therefore inhibition of Chromosome 12 Open Reading Frame 22 (C12orf22, Accession NM\_030809). Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C12orf22. FLJ10687 (Accession NM\_018178) is another VGAM1545 host target gene. FLJ10687 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ10687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10687 BINDING SITE, designated SEQ ID:20009, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53040] Another function of VGAM1545 is therefore inhibition of FLJ10687 (Accession NM\_018178). Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10687. FLJ21140 (Accession NM\_024776) is another VGAM1545 host target gene. FLJ21140 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21140 BINDING SITE, designated SEQ ID:24143, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53041] Another function of VGAM1545 is therefore inhibition of FLJ21140 (Accession NM\_024776). Accordingly, utilities of

VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21140. KIAA0872 (Accession NM\_014940) is another VGAM1545 host target gene. KIAA0872 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0872 BINDING SITE, designated SEQ ID:17247, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53042] Another function of VGAM1545 is therefore inhibition of KIAA0872 (Accession NM\_014940). Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0872. KIAA1211 (Accession XM\_044178) is another VGAM1545 host target gene. KIAA1211 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1211 BINDING SITE, designated SEQ ID:34161, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53043] Another function of VGAM1545 is therefore inhibition of KIAA1211 (Accession XM\_044178). Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1211. R3H Domain (binds single-stranded nucleic acids) Containing (R3HDM, Accession NM\_015361) is another VGAM1545 host target gene. R3HDM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by R3HDM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of R3HDM BINDING SITE, designated SEQ ID:17663, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53044] Another function of VGAM1545 is therefore inhibition of R3H Domain (binds single-stranded nucleic acids) Containing (R3HDM, Accession NM\_015361). Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with R3HDM. LOC148946 (Accession XM\_097557) is another VGAM1545 host target gene. LOC148946 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148946, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148946 BINDING SITE, designated SEQ ID:40941, to the nucleotide sequence of VGAM1545 RNA, herein designated VGAM RNA, also designated SEQ ID:4256.

[53045] Another function of VGAM1545 is therefore inhibition of LOC148946 (Accession XM\_097557). Accordingly, utilities of VGAM1545 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148946. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1546 (VGAM1546) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53046] VGAM1546 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.



The method by which VGAM1546 was detected is described hereinabove with reference to Figs. 1–8.

[53047] VGAM1546 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus.

VGAM1546 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53048] VGAM1546 gene encodes a VGAM1546 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1546 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1546 precursor RNA is designated SEQ ID:1532, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1532 is located at position 51253 relative to the genome of Variola Virus.

[53049] VGAM1546 precursor RNA folds onto itself, forming VGAM1546 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53050] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1546 folded precursor RNA into VGAM1546 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1546 RNA is designated SEQ ID:4257, and is provided hereinbelow with reference to the sequence listing part.

[53051] VGAM1546 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1546 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1546 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53052] VGAM1546 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1546 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1546 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1546 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1546 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[53053] The complementary binding of VGAM1546 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1546 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1546 host target RNA into VGAM1546 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53054] It is appreciated that VGAM1546 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1546 host target genes. The mRNA of each one of this plurality of VGAM1546 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1546 RNA, herein designated VGAM RNA, and which when bound by VGAM1546 RNA causes inhibition of translation of respective one or more VGAM1546 host target proteins.

[53055] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1546 gene, herein designated VGAM GENE, on one or more VGAM1546 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53056] It is yet further appreciated that a function of VGAM1546 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1546 correlate with, and may be deduced from, the identity of the host target genes which VGAM1546 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53057] Nucleotide sequences of the VGAM1546 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1546 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1546 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1546 are further described hereinbelow with reference to Table 1.

[53058] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1546 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1546 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53059] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1546 gene, herein designated VGAM is inhibition of expression of VGAM1546 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1546 correlate with, and may be deduced from, the identity of the target genes which VGAM1546 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53060] Caveolin 3 (CAV3, Accession NM\_033337) is a VGAM1546 host target gene. CAV3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAV3, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAV3 BINDING SITE, designated SEQ ID:27190, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53061] A function of VGAM1546 is therefore inhibition of Caveolin 3 (CAV3, Accession NM\_033337). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAV3. CD1D Antigen, D Polypeptide (CD1D, Accession XM\_086610) is another VGAM1546 host target gene. CD1D BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CD1D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD1D BINDING SITE, designated SEQ ID:38789, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53062] Another function of VGAM1546 is therefore inhibition of CD1D Antigen, D Polypeptide (CD1D, Accession XM\_086610), a gene which is a member D of the CD1

family; involved in antigen presentation . Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD1D. The function of CD1D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1107. COX10 Homolog, Cytochrome C Oxidase Assembly Protein, Heme A: Farnesyltransferase (yeast) (COX10, Accession NM\_001303) is another VGAM1546 host target gene. COX10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COX10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX10 BINDING SITE, designated SEQ ID:6979, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53063] Another function of VGAM1546 is therefore inhibition of COX10 Homolog, Cytochrome C Oxidase Assembly Protein, Heme A: Farnesyltransferase (yeast) (COX10, Accession NM\_001303). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and



clinical conditions associated with COX10. Jerky Homolog-like (mouse) (JRKL, Accession NM\_003772) is another VGAM1546 host target gene. JRKL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JRKL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JRKL BINDING SITE, designated SEQ ID:9854, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53064] Another function of VGAM1546 is therefore inhibition of Jerky Homolog-like (mouse) (JRKL, Accession NM\_003772), a gene which is a Jerky-related protein and similar to centromere binding protein-B and other nuclear regulators. Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JRKL. The function of JRKL has been established by previous studies. Toth et al. (1995) found that inactivation of the mouse 'jerky' gene results in epileptic seizures. See 603210. Zeng et al. (1997) identified a human tonsil cDNA encoding a protein similar to jerky. They designated the predicted 442-amino acid pro-

tein HHMJG (human homolog of mouse jerky gene). The HHMJG and mouse jerky proteins are 35% identical. Northern blot analysis revealed that HHMJG is abundantly expressed as a 4-kb mRNA in various tissues. In testis, an additional 2-kb transcript is present. By fluorescence in situ hybridization, Zeng et al. (1997) mapped the HHMJG gene to 11q21.

[53065] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53066] Toth, M.; Grimsby, J.; Buzsaki, G.; Donovan, G. P. : Epileptic seizures caused by inactivation of a novel gene, jerky, related to centromere binding protein-B in transgenic mice. *Nature Genet.* 11: 71–75, 1995. Note: Erratum: *Nature Genet.* 12: 110 only, 1996. ; and

[53067] Zeng, Z.; Kyaw, H.; Gakenheimer, K. R.; Augustus, M.; Fan, P.; Zhang, X.; Su, K.; Carter, K. C.; Li, Y. : Cloning, mapping, and tissue distribution of a human homologue of the mouse jerk.

[53068] Further studies establishing the function and utilities of JRKL are found in John Hopkins OMIM database record ID 603211, and in cited publications numbered 5438–5439 listed in the bibliography section hereinbelow, which are

also hereby incorporated by reference. Microtubule-associated Protein 7 (MAP7, Accession NM\_003980) is another VGAM1546 host target gene. MAP7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP7 BINDING SITE, designated SEQ ID:10116, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53069] Another function of VGAM1546 is therefore inhibition of Microtubule-associated Protein 7 (MAP7, Accession NM\_003980), a gene which Microtubule-associated protein 7; stabilizes microtubules, may help establish epithelial cell polarity. Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP7. The function of MAP7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1373. Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM\_002507) is another VGAM1546 host

target gene. NGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGFR BINDING SITE, designated SEQ ID:8329, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53070] Another function of VGAM1546 is therefore inhibition of Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM\_002507), a gene which can mediate cell survival as well as cell death of neural cells. Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGFR. The function of NGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM212.CNIL (Accession NM\_005776) is another VGAM1546 host target gene. CNIL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNIL, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNIL BINDING SITE, designated SEQ ID:12352, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53071] Another function of VGAM1546 is therefore inhibition of CNIL (Accession NM\_005776). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNIL. FLJ10154 (Accession NM\_018011) is another VGAM1546 host target gene. FLJ10154 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10154 BINDING SITE, designated SEQ ID:19745, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53072] Another function of VGAM1546 is therefore inhibition of FLJ10154 (Accession NM\_018011). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10154. FLJ10607 (Accession XM\_085119) is another VGAM1546 host target gene. FLJ10607 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10607, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10607 BINDING SITE, designated SEQ ID:37834, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53073] Another function of VGAM1546 is therefore inhibition of FLJ10607 (Accession XM\_085119). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10607. FLJ20189 (Accession NM\_017704) is another VGAM1546 host target gene. FLJ20189 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20189 BINDING SITE, designated SEQ ID:19278, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM

RNA, also designated SEQ ID:4257.

[53074] Another function of VGAM1546 is therefore inhibition of FLJ20189 (Accession NM\_017704). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20189. KIAA1237 (Accession XM\_087386) is another VGAM1546 host target gene. KIAA1237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1237 BINDING SITE, designated SEQ ID:39217, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53075] Another function of VGAM1546 is therefore inhibition of KIAA1237 (Accession XM\_087386). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1237. KIAA1573 (Accession XM\_031545) is another VGAM1546 host target gene. KIAA1573 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1573, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1573 BINDING SITE, designated SEQ ID:31413, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53076] Another function of VGAM1546 is therefore inhibition of KIAA1573 (Accession XM\_031545). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1573. KIAA1579 (Accession NM\_018211) is another VGAM1546 host target gene. KIAA1579 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1579, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1579 BINDING SITE, designated SEQ ID:20118, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53077] Another function of VGAM1546 is therefore inhibition of KIAA1579 (Accession NM\_018211). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with KIAA1579. Oxysterol Binding Protein-like 8 (OSBPL8, Accession NM\_020841) is another VGAM1546 host target gene. OSBPL8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL8 BINDING SITE, designated SEQ ID:21903, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53078] Another function of VGAM1546 is therefore inhibition of Oxysterol Binding Protein-like 8 (OSBPL8, Accession NM\_020841). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL8. P21 (CDKN1A)-activated Kinase 2 (PAK2, Accession XM\_039354) is another VGAM1546 host target gene. PAK2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PAK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of PAK2 BINDING SITE, designated SEQ ID:33061, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53079] Another function of VGAM1546 is therefore inhibition of P21 (CDKN1A)-activated Kinase 2 (PAK2, Accession XM\_039354). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK2. RAB33B, Member RAS Oncogene Family (RAB33B, Accession NM\_031296) is another VGAM1546 host target gene. RAB33B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB33B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB33B BINDING SITE, designated SEQ ID:25328, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53080] Another function of VGAM1546 is therefore inhibition of RAB33B, Member RAS Oncogene Family (RAB33B, Accession NM\_031296). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with RAB33B. Transducer of ERBB2, 2 (TOB2, Accession XM\_170995) is another VGAM1546 host target gene. TOB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOB2 BINDING SITE, designated SEQ ID:45760, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53081] Another function of VGAM1546 is therefore inhibition of Transducer of ERBB2, 2 (TOB2, Accession XM\_170995). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOB2. LOC158038 (Accession XM\_088446) is another VGAM1546 host target gene. LOC158038 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158038 BINDING SITE, desig-

nated SEQ ID:39699, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53082] Another function of VGAM1546 is therefore inhibition of LOC158038 (Accession XM\_088446). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158038. LOC51141 (Accession XM\_043953) is another VGAM1546 host target gene. LOC51141 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51141, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51141 BINDING SITE, designated SEQ ID:34047, to the nucleotide sequence of VGAM1546 RNA, herein designated VGAM RNA, also designated SEQ ID:4257.

[53083] Another function of VGAM1546 is therefore inhibition of LOC51141 (Accession XM\_043953). Accordingly, utilities of VGAM1546 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51141. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1547 (VGAM1547) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53084] VGAM1547 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1547 was detected is described hereinabove with reference to Figs. 1–8.

[53085] VGAM1547 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia Virus. VGAM1547 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53086] VGAM1547 gene encodes a VGAM1547 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1547 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1547 precursor RNA is designated SEQ ID:1533, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1533 is located at position 64695 relative to the

genome of Vaccinia Virus.

[53087] VGAM1547 precursor RNA folds onto itself, forming VGAM1547 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53088] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1547 folded precursor RNA into VGAM1547 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1547 RNA is designated SEQ ID:4258, and is provided hereinbelow with reference to the sequence listing part.

[53089] VGAM1547 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1547 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1547 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[53090] VGAM1547 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1547 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1547 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1547 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1547 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53091] The complementary binding of VGAM1547 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1547 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1547 host target RNA into VGAM1547 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53092] It is appreciated that VGAM1547 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1547 host target genes. The mRNA of each one of this plurality of VGAM1547 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1547 RNA, herein designated VGAM RNA, and which when bound by VGAM1547 RNA causes inhibition of translation of respective one or more VGAM1547 host target proteins.



[53093] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1547 gene, herein designated VGAM GENE, on one or more VGAM1547 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53094] It is yet further appreciated that a function of VGAM1547 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGAM1547 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1547 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53095] Nucleotide sequences of the VGAM1547 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1547 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1547 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1547 are further described hereinbelow with reference to Table 1.

[53096] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1547 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1547 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53097] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1547 gene, herein designated VGAM is inhibition of expression of VGAM1547 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1547 correlate with, and may be deduced

from, the identity of the target genes which VGAM1547 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53098] Apical Protein-like (*Xenopus laevis*) (APXL, Accession NM\_001649) is a VGAM1547 host target gene. APXL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APXL BINDING SITE, designated SEQ ID:7352, to the nucleotide sequence of VGAM1547 RNA, herein designated VGAM RNA, also designated SEQ ID:4258.

[53099] A function of VGAM1547 is therefore inhibition of Apical Protein-like (*Xenopus laevis*) (APXL, Accession NM\_001649), a gene which is implicated in amiloride-sensitive sodium channel activity. Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APXL. The function of APXL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152.Cockayne Syndrome 1 (classical) (CKN1, Ac-

cession NM\_000082) is another VGAM1547 host target gene. CKN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKN1 BINDING SITE, designated SEQ ID:5529, to the nucleotide sequence of VGAM1547 RNA, herein designated VGAM RNA, also designated SEQ ID:4258.

[53100] Another function of VGAM1547 is therefore inhibition of Cockayne Syndrome 1 (classical) (CKN1, Accession NM\_000082). Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKN1. High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483) is another VGAM1547 host target gene. HMGA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGA2 BINDING SITE, designated SEQ ID:9561, to the nucleotide sequence of VGAM1547 RNA, herein designated VGAM

RNA, also designated SEQ ID:4258.

[53101] Another function of VGAM1547 is therefore inhibition of High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483), a gene which may affect transcription and cell differentiation; shares common DNA-binding motif with other HMG HMG I/Y family members. Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGA2. The function of HMGA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Zinc Finger Protein 36 (K0X18) (ZNF36, Accession XM\_168302) is another VGAM1547 host target gene. ZNF36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF36 BINDING SITE, designated SEQ ID:45101, to the nucleotide sequence of VGAM1547 RNA, herein designated VGAM RNA, also designated SEQ ID:4258.

[53102] Another function of VGAM1547 is therefore inhibition of

Zinc Finger Protein 36 (K0X 18) (ZNF36, Accession XM\_168302), a gene which may be involved in transcriptional regulation. Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF36. The function of ZNF36 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM804.FLJ23191 (Accession NM\_024574) is another VGAM1547 host target gene. FLJ23191 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23191 BINDING SITE, designated SEQ ID:23803, to the nucleotide sequence of VGAM1547 RNA, herein designated VGAM RNA, also designated SEQ ID:4258.

[53103] Another function of VGAM1547 is therefore inhibition of FLJ23191 (Accession NM\_024574). Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23191. KIAA0841 (Accession XM\_049237) is another

VGAM1547 host target gene. KIAA0841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0841 BINDING SITE, designated SEQ ID:35359, to the nucleotide sequence of VGAM1547 RNA, herein designated VGAM RNA, also designated SEQ ID:4258.

[53104] Another function of VGAM1547 is therefore inhibition of KIAA0841 (Accession XM\_049237). Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0841. Ring Finger Protein 20 (RNF20, Accession NM\_019592) is another VGAM1547 host target gene. RNF20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF20 BINDING SITE, designated SEQ ID:21213, to the nucleotide sequence of VGAM1547 RNA, herein designated VGAM RNA, also designated SEQ

ID:4258.

[53105] Another function of VGAM1547 is therefore inhibition of Ring Finger Protein 20 (RNF20, Accession NM\_019592). Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF20. LOC118851 (Accession XM\_061180) is another VGAM1547 host target gene. LOC118851 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC118851, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118851 BINDING SITE, designated SEQ ID:37199, to the nucleotide sequence of VGAM1547 RNA, herein designated VGAM RNA, also designated SEQ ID:4258.

[53106] Another function of VGAM1547 is therefore inhibition of LOC118851 (Accession XM\_061180). Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118851. LOC150005 (Accession XM\_097795) is another VGAM1547 host target gene. LOC150005 BINDING SITE is HOST TARGET binding site found in the 3' un-



translated region of mRNA encoded by LOC150005, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150005 BINDING SITE, designated SEQ ID:41122, to the nucleotide sequence of VGAM1547 RNA, herein designated VGAM RNA, also designated SEQ ID:4258.

[53107] Another function of VGAM1547 is therefore inhibition of LOC150005 (Accession XM\_097795). Accordingly, utilities of VGAM1547 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150005. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1548 (VGAM1548) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53108] VGAM1548 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1548 was detected is described hereinabove with reference to Figs. 1-8.

[53109] VGAM1548 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1548 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53110] VGAM1548 gene encodes a VGAM1548 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1548 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1548 precursor RNA is designated SEQ ID:1534, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1534 is located at position 113488 relative to the genome of Macaca Mulatta Rhadinovirus.

[53111] VGAM1548 precursor RNA folds onto itself, forming VGAM1548 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53112] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1548 folded precursor RNA into VGAM1548 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1548 RNA is designated SEQ ID:4259, and is provided hereinbelow with reference to the sequence listing part.

[53113] VGAM1548 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1548 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1548 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53114] VGAM1548 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1548 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1548 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1548 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1548 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53115] The complementary binding of VGAM1548 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1548 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1548

host target RNA into VGAM1548 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53116] It is appreciated that VGAM1548 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1548 host target genes. The mRNA of each one of this plurality of VGAM1548 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1548 RNA, herein designated VGAM RNA, and which when bound by VGAM1548 RNA causes inhibition of translation of respective one or more VGAM1548 host target proteins.

[53117] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1548 gene, herein designated VGAM GENE, on one or more VGAM1548 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53118] It is yet further appreciated that a function of VGAM1548 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1548 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1548 correlate with, and may be deduced from, the identity of the host target genes which VGAM1548 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53119] Nucleotide sequences of the VGAM1548 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1548 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1548 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1548 are further

described hereinbelow with reference to Table 1.

[53120] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1548 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1548 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53121] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1548 gene, herein designated VGAM is inhibition of expression of VGAM1548 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1548 correlate with, and may be deduced from, the identity of the target genes which VGAM1548 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53122] LOC92249 (Accession XM\_043814) is a VGAM1548 host target gene. LOC92249 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92249 BINDING SITE,

designated SEQ ID:34020, to the nucleotide sequence of VGAM1548 RNA, herein designated VGAM RNA, also designated SEQ ID:4259.

[53123] A function of VGAM1548 is therefore inhibition of LOC92249 (Accession XM\_043814). Accordingly, utilities of VGAM1548 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1549 (VGAM1549) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53124] VGAM1549 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1549 was detected is described hereinabove with reference to Figs. 1–8.

[53125] VGAM1549 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1549 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.



[53126] VGAM1549 gene encodes a VGAM1549 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1549 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1549 precursor RNA is designated SEQ ID:1535, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1535 is located at position 117267 relative to the genome of Macaca Mulatta Rhadinovirus.

[53127] VGAM1549 precursor RNA folds onto itself, forming VGAM1549 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53128] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1549 folded precursor RNA into VGAM1549 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 58%) nucleotide sequence of VGAM1549 RNA is designated SEQ ID:4260, and is provided hereinbelow with reference to the sequence listing part.

[53129] VGAM1549 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1549 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1549 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53130] VGAM1549 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1549 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1549 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1549 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1549 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53131] The complementary binding of VGAM1549 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1549 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1549 host target RNA into VGAM1549 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53132] It is appreciated that VGAM1549 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1549 host target genes. The mRNA of each one of this plurality of VGAM1549 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1549 RNA, herein designated VGAM RNA, and which when bound by VGAM1549 RNA causes inhibition of translation of respective one or more VGAM1549 host target proteins.

[53133] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1549 gene, herein designated VGAM GENE, on one or more VGAM1549 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[53134] It is yet further appreciated that a function of VGAM1549 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1549 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1549 correlate with, and may be deduced from, the identity of the host target genes which VGAM1549 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53135] Nucleotide sequences of the VGAM1549 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1549 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1549 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1549 are further described hereinbelow with reference to Table 1.

[53136] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1549 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1549 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53137] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1549 gene, herein designated VGAM is inhibition of expression of VGAM1549 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1549 correlate with, and may be deduced from, the identity of the target genes which VGAM1549 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53138] Msh Homeo Box Homolog 2 (Drosophila) (MSX2, Accession XM\_037646) is a VGAM1549 host target gene. MSX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSX2 BINDING SITE, designated SEQ ID:32660, to the nucleotide sequence of VGAM1549 RNA, herein designated VGAM RNA, also designated SEQ ID:4260.

[53139] A function of VGAM1549 is therefore inhibition of Msh

Homeo Box Homolog 2 (Drosophila) (MSX2, Accession XM\_037646). Accordingly, utilities of VGAM1549 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSX2. FLJ10244 (Accession NM\_018037) is another VGAM1549 host target gene. FLJ10244 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10244, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10244 BINDING SITE, designated SEQ ID:19780, to the nucleotide sequence of VGAM1549 RNA, herein designated VGAM RNA, also designated SEQ ID:4260.

[53140] Another function of VGAM1549 is therefore inhibition of FLJ10244 (Accession NM\_018037). Accordingly, utilities of VGAM1549 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10244. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1550 (VGAM1550) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[53141] VGAM1550 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1550 was detected is described hereinabove with reference to Figs. 1-8.

[53142] VGAM1550 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1550 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53143] VGAM1550 gene encodes a VGAM1550 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1550 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1550 precursor RNA is designated SEQ ID:1536, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1536 is located at position 114505 relative to the genome of Macaca Mulatta Rhadinovirus.

[53144] VGAM1550 precursor RNA folds onto itself, forming VGAM1550 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53145] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1550 folded precursor RNA into VGAM1550 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1550 RNA is designated SEQ ID:4261, and is provided hereinbelow with reference to the sequence listing part.

[53146] VGAM1550 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1550 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1550 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53147] VGAM1550 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1550 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1550 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1550 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1550 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53148] The complementary binding of VGAM1550 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1550 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1550 host target RNA into VGAM1550 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53149] It is appreciated that VGAM1550 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1550 host target genes. The mRNA of each one of this plurality of VGAM1550 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1550 RNA, herein designated VGAM RNA, and which when bound by VGAM1550 RNA causes inhibition of translation of respective one or more VGAM1550 host target proteins.

[53150] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1550 gene, herein designated VGAM GENE, on one or more VGAM1550 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53151] It is yet further appreciated that a function of VGAM1550 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1550 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1550 correlate with, and may be deduced from, the identity of the host target genes which VGAM1550 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[53152] Nucleotide sequences of the VGAM1550 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1550 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1550 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1550 are further described hereinbelow with reference to Table 1.

[53153] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1550 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1550 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53154] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1550 gene, herein designated VGAM is inhibition of expression of VGAM1550 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1550 correlate with, and may be deduced from, the identity of the target genes which VGAM1550 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53155] Vinculin (VCL, Accession NM\_003373) is a VGAM1550 host target gene. VCL BINDING SITE1 and VCL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by VCL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VCL BINDING SITE1 and VCL BINDING SITE2, designated SEQ ID:9401 and SEQ ID:15190 respectively, to the nucleotide sequence of VGAM1550 RNA, herein designated VGAM RNA, also designated SEQ ID:4261.

[53156] A function of VGAM1550 is therefore inhibition of Vinculin (VCL, Accession NM\_003373). Accordingly, utilities of VGAM1550 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VCL. LOC145231 (Accession XM\_096740) is another VGAM1550 host target gene. LOC145231 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145231 BINDING SITE, designated SEQ ID:40519, to

the nucleotide sequence of VGAM1550 RNA, herein designated VGAM RNA, also designated SEQ ID:4261.

[53157] Another function of VGAM1550 is therefore inhibition of LOC145231 (Accession XM\_096740). Accordingly, utilities of VGAM1550 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145231. LOC221398 (Accession XM\_165762) is another VGAM1550 host target gene. LOC221398 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221398, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221398 BINDING SITE, designated SEQ ID:43750, to the nucleotide sequence of VGAM1550 RNA, herein designated VGAM RNA, also designated SEQ ID:4261.

[53158] Another function of VGAM1550 is therefore inhibition of LOC221398 (Accession XM\_165762). Accordingly, utilities of VGAM1550 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221398. LOC90594 (Accession XM\_032820) is another VGAM1550 host target gene. LOC90594 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC90594, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90594 BINDING SITE, designated SEQ ID:31774, to the nucleotide sequence of VGAM1550 RNA, herein designated VGAM RNA, also designated SEQ ID:4261.

[53159] Another function of VGAM1550 is therefore inhibition of LOC90594 (Accession XM\_032820). Accordingly, utilities of VGAM1550 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90594. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1551 (VGAM1551) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53160] VGAM1551 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1551 was detected is described hereinabove with reference to Figs. 1-8.

[53161] VGAM1551 gene, herein designated VGAM GENE, is a viral



gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1551 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53162] VGAM1551 gene encodes a VGAM1551 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1551 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1551 precursor RNA is designated SEQ ID:1537, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1537 is located at position 113655 relative to the genome of Macaca Mulatta Rhadinovirus.

[53163] VGAM1551 precursor RNA folds onto itself, forming VGAM1551 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53164] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1551 folded precursor RNA into VGAM1551 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1551 RNA is designated SEQ ID:4262, and is provided hereinbelow with reference to the sequence listing part.

[53165] VGAM1551 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1551 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1551 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53166] VGAM1551 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1551 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1551 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1551 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1551 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53167] The complementary binding of VGAM1551 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1551 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1551

host target RNA into VGAM1551 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53168] It is appreciated that VGAM1551 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1551 host target genes. The mRNA of each one of this plurality of VGAM1551 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1551 RNA, herein designated VGAM RNA, and which when bound by VGAM1551 RNA causes inhibition of translation of respective one or more VGAM1551 host target proteins.

[53169] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1551 gene, herein designated VGAM GENE, on one or more VGAM1551 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53170] It is yet further appreciated that a function of VGAM1551 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1551 correlate with, and may be deduced from, the identity of the host target genes which VGAM1551 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53171] Nucleotide sequences of the VGAM1551 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1551 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1551 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1551 are further

described hereinbelow with reference to Table 1.

[53172] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1551 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1551 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53173] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1551 gene, herein designated VGAM is inhibition of expression of VGAM1551 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1551 correlate with, and may be deduced from, the identity of the target genes which VGAM1551 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53174] Calcium Channel, Voltage-dependent, Gamma Subunit 3 (CACNG3, Accession NM\_006539) is a VGAM1551 host target gene. CACNG3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CACNG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of CACNG3 BINDING SITE, designated SEQ ID:13292, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53175] A function of VGAM1551 is therefore inhibition of Calcium Channel, Voltage-dependent, Gamma Subunit 3 (CACNG3, Accession NM\_006539), a gene which is thought to stabilize the calcium channel in an inactivated state. Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNG3. The function of CACNG3 has been established by previous studies. Voltage-dependent calcium channels couple membrane depolarization in a number of cellular processes. These activities are regulated by distinct channels composed of alpha-1 (e.g., CACNA1D; 114206), beta (e.g., CACNB1; 114207), alpha-2/delta (e.g., CACNA2D1; 114204), and gamma (e.g., CACNG1; 114209) subunits. By genomic sequence analysis, Black and Lennon (1999) and Burgess et al. (1999) determined that the CACNG3 gene contains 4 exons with a large first intron.

[53176] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

[53177] Black, J. L., III; Lennon, V. A. : Identification and cloning of putative human neuronal voltage-gated calcium channel gamma-2 and gamma-3 subunits: neurologic implications. Mayo Clin. Proc. 74: 357-361, 1999. ; and

[53178] Burgess, D. L.; Davis, C. F.; Gefrides, L. A.; Noebels, J. L. : Identification of three novel Ca(2+) channel gamma subunit genes reveals molecular diversification by tandem and chromoso.

[53179] Further studies establishing the function and utilities of CACNG3 are found in John Hopkins OMIM database record ID 606403, and in cited publications numbered 6188-4526 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Golgi Re-assembly Stacking Protein 1, 65kDa (GORASP1, Accession NM\_031899) is another VGAM1551 host target gene. GORASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GORASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GORASP1 BINDING SITE, designated SEQ ID:25646, to the nucleotide sequence of VGAM1551 RNA,



herein designated VGAM RNA, also designated SEQ ID:4262.

[53180] Another function of VGAM1551 is therefore inhibition of Golgi Reassembly Stacking Protein 1, 65kDa (GORASP1, Accession NM\_031899), a gene which has some function with the Golgi apparatus. Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GORASP1. The function of GORASP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM630. Leukemia Inhibitory Factor Receptor (LIFR, Accession NM\_002310) is another VGAM1551 host target gene. LIFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIFR BINDING SITE, designated SEQ ID:8100, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53181] Another function of VGAM1551 is therefore inhibition of

Leukemia Inhibitory Factor Receptor (LIFR, Accession NM\_002310). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIFR. Protein Phosphatase 2, Regulatory Subunit B (B56), Delta Isoform (PPP2R5D, Accession NM\_006245) is another VGAM1551 host target gene. PPP2R5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP2R5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R5D BINDING SITE, designated SEQ ID:12918, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53182] Another function of VGAM1551 is therefore inhibition of Protein Phosphatase 2, Regulatory Subunit B (B56), Delta Isoform (PPP2R5D, Accession NM\_006245), a gene which is a regulatory subunit of protein phosphatase 2A. Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R5D. The function of PPP2R5D and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM96. Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM\_114191) is another VGAM1551 host target gene. C21orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf108 BINDING SITE, designated SEQ ID:42772, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53183] Another function of VGAM1551 is therefore inhibition of Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM\_114191). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf108. KIAA1161 (Accession XM\_088501) is another VGAM1551 host target gene. KIAA1161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1161, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1161 BINDING SITE, designated SEQ ID:39751, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53184] Another function of VGAM1551 is therefore inhibition of KIAA1161 (Accession XM\_088501). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1161. KIAA1862 (Accession XM\_044212) is another VGAM1551 host target gene. KIAA1862 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1862, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1862 BINDING SITE, designated SEQ ID:34176, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53185] Another function of VGAM1551 is therefore inhibition of KIAA1862 (Accession XM\_044212). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1862. LOC148936 (Accession XM\_097556) is another VGAM1551 host target gene. LOC148936 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148936 BINDING SITE, designated SEQ ID:40930, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53186] Another function of VGAM1551 is therefore inhibition of LOC148936 (Accession XM\_097556). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148936. LOC148938 (Accession XM\_097555) is another VGAM1551 host target gene. LOC148938 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148938, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148938 BINDING SITE, designated SEQ ID:40923, to the nucleotide sequence of VGAM1551 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4262.

[53187] Another function of VGAM1551 is therefore inhibition of LOC148938 (Accession XM\_097555). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148938. LOC157273 (Accession XM\_098743) is another VGAM1551 host target gene. LOC157273 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157273 BINDING SITE, designated SEQ ID:41782, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53188] Another function of VGAM1551 is therefore inhibition of LOC157273 (Accession XM\_098743). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157273. LOC254057 (Accession XM\_173085) is another VGAM1551 host target gene. LOC254057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254057, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254057 BINDING SITE, designated SEQ ID:46350, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53189] Another function of VGAM1551 is therefore inhibition of LOC254057 (Accession XM\_173085). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254057. LOC255465 (Accession XM\_173206) is another VGAM1551 host target gene. LOC255465 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255465 BINDING SITE, designated SEQ ID:46449, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53190] Another function of VGAM1551 is therefore inhibition of LOC255465 (Accession XM\_173206). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC255465. LOC91947 (Accession XM\_041721) is another VGAM1551 host target gene. LOC91947 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91947, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91947 BINDING SITE, designated SEQ ID:33571, to the nucleotide sequence of VGAM1551 RNA, herein designated VGAM RNA, also designated SEQ ID:4262.

[53191] Another function of VGAM1551 is therefore inhibition of LOC91947 (Accession XM\_041721). Accordingly, utilities of VGAM1551 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91947. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1552 (VGAM1552) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53192] VGAM1552 is a novel bioinformatically detected regula-



tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1552 was detected is described hereinabove with reference to Figs. 1–8.

[53193] VGAM1552 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1552 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53194] VGAM1552 gene encodes a VGAM1552 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1552 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1552 precursor RNA is designated SEQ ID:1538, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1538 is located at position 116594 relative to the genome of Macaca Mulatta Rhadinovirus.

[53195] VGAM1552 precursor RNA folds onto itself, forming VGAM1552 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53196] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1552 folded precursor RNA into VGAM1552 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1552 RNA is designated SEQ ID:4263, and is provided hereinbelow with reference to the sequence listing part.

[53197] VGAM1552 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1552 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1552 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53198] VGAM1552 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1552 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1552 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1552 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1552 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53199] The complementary binding of VGAM1552 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1552 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1552 host target RNA into VGAM1552 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53200] It is appreciated that VGAM1552 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1552 host target genes. The mRNA of each one of this plurality of VGAM1552 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1552 RNA, herein designated VGAM RNA, and which when bound by VGAM1552 RNA causes inhibition of translation of respective one or more VGAM1552 host target proteins.

[53201] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1552 gene, herein designated VGAM GENE, on one or more VGAM1552 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53202] It is yet further appreciated that a function of VGAM1552 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1552 correlate with, and may be deduced from, the identity of the host target genes which VGAM1552 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53203] Nucleotide sequences of the VGAM1552 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1552 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1552 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1552 are further described hereinbelow with reference to Table 1.

[53204] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1552 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1552 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53205] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1552 gene, herein designated VGAM is inhibition of expression of VGAM1552 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1552 correlate with, and may be deduced from, the identity of the target genes which VGAM1552 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53206] Cadherin Related 23 (CDH23, Accession NM\_022124) is a VGAM1552 host target gene. CDH23 BINDING SITE1 and CDH23 BINDING SITE2 are HOST TARGET binding sites

found in untranslated regions of mRNA encoded by CDH23, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH23 BINDING SITE1 and CDH23 BINDING SITE2, designated SEQ ID:22671 and SEQ ID:27419 respectively, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53207] A function of VGAM1552 is therefore inhibition of Cadherin Related 23 (CDH23, Accession NM\_022124). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH23. Inositol Polyphosphate-4-phosphatase, Type I, 107kDa (INPP4A, Accession NM\_001566) is another VGAM1552 host target gene. INPP4A BINDING SITE1 and INPP4A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by INPP4A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP4A BINDING SITE1 and INPP4A BINDING SITE2, designated SEQ ID:7295

and SEQ ID:10247 respectively, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53208] Another function of VGAM1552 is therefore inhibition of Inositol Polyphosphate-4-phosphatase, Type I, 107kDa (INPP4A, Accession NM\_001566), a gene which catalyzes the hydrolysis of the 4-position phosphate of inositol 3,4-bisphosphate and inositol 1,3,4-trisphosphate. Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP4A. The function of INPP4A has been established by previous studies. Inositol polyphosphate 4-phosphatase catalyzes the hydrolysis of the 4-position phosphate of inositol 3,4-bisphosphate and inositol 1,3,4-trisphosphate. It also catalyzes, at a much higher rate, the hydrolysis of the 4-position phosphate of phosphatidylinositol 3,4-bisphosphate. Norris et al. (1995) noted that the latter activity has been implicated in mitogenesis mediated by PDGF receptor, the oxidative burst of neutrophils, and translocation of the glucose transporter to the plasma membrane. Norris et al. (1995) purified the enzyme from rat brain and obtained partial amino acid sequence from which degenerate primers were designed.



A PCR product was obtained and used to isolate a 5,607-bp composite cDNA which encodes a 939-amino acid reading frame from the rat. The authors screened a human brain cDNA library and identified a sequence that predicts a 938-amino acid protein which is 97% identical to the rat protein. Recombinant protein was shown to have the appropriate enzymatic activity. Northern blots indicated that, in the rat, the gene is widely expressed with highest levels in the brain, heart, and skeletal muscle

[53209] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53210] Joseph, R. E.; Walker, J.; Norris, F. A. : Assignment of the inositol polyphosphate 4-phosphatase type I gene (INPP4A) to human chromosome band 2q11.2 by in situ hybridization. *Cytogenet. Cell Genet.* 87: 276-277, 1999.  
; and

[53211] Norris, F. A.; Auethavekiat, V.; Majerus, P. W. : The isolation and characterization of cDNA encoding human and rat brain inositol polyphosphate 4-phosphatase. *J. Biol. Chem.* 270: 16128.

[53212] Further studies establishing the function and utilities of INPP4A are found in John Hopkins OMIM database record

ID 600916, and in cited publications numbered 9612–9613 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Topoisomerase (DNA) III Beta (TOP3B, Accession NM\_003935) is another VGAM1552 host target gene. TOP3B BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TOP3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOP3B BINDING SITE, designated SEQ ID:10038, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53213] Another function of VGAM1552 is therefore inhibition of Topoisomerase (DNA) III Beta (TOP3B, Accession NM\_003935). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOP3B. Ubiquitin Specific Protease 1 (USP1, Accession NM\_003368) is another VGAM1552 host target gene. USP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by USP1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP1 BINDING SITE, designated SEQ ID:9392, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53214] Another function of VGAM1552 is therefore inhibition of Ubiquitin Specific Protease 1 (USP1, Accession NM\_003368). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP1. XT3 (Accession NM\_020208) is another VGAM1552 host target gene. XT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XT3 BINDING SITE, designated SEQ ID:21439, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53215] Another function of VGAM1552 is therefore inhibition of XT3 (Accession NM\_020208), a gene which is a Kidney-specific orphan transporter. Accordingly, utilities of

VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XT3. The function of XT3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM21. Chromosome 20 Open Reading Frame 39 (C20orf39, Accession NM\_024893) is another VGAM1552 host target gene. C20orf39 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf39 BINDING SITE, designated SEQ ID:24369, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53216] Another function of VGAM1552 is therefore inhibition of Chromosome 20 Open Reading Frame 39 (C20orf39, Accession NM\_024893). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf39. EHM2 (Accession NM\_019114) is another VGAM1552 host target gene. EHM2 BINDING SITE is HOST TARGET binding site

found in the 5` untranslated region of mRNA encoded by EHM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EHM2 BINDING SITE, designated SEQ ID:21189, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53217] Another function of VGAM1552 is therefore inhibition of EHM2 (Accession NM\_019114). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EHM2. FLJ10116 (Accession NM\_018000) is another VGAM1552 host target gene. FLJ10116 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10116 BINDING SITE, designated SEQ ID:19727, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53218] Another function of VGAM1552 is therefore inhibition of FLJ10116 (Accession NM\_018000). Accordingly, utilities of

VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10116. KIAA0217 (Accession XM\_040265) is another VGAM1552 host target gene. KIAA0217 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0217, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0217 BINDING SITE, designated SEQ ID:33283, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53219] Another function of VGAM1552 is therefore inhibition of KIAA0217 (Accession XM\_040265). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0217. KIAA0427 (Accession NM\_014772) is another VGAM1552 host target gene. KIAA0427 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0427 BINDING SITE, designated SEQ ID:16577, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53220] Another function of VGAM1552 is therefore inhibition of KIAA0427 (Accession NM\_014772). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0427. KIAA0618 (Accession NM\_014833) is another VGAM1552 host target gene. KIAA0618 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0618 BINDING SITE, designated SEQ ID:16836, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53221] Another function of VGAM1552 is therefore inhibition of KIAA0618 (Accession NM\_014833). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0618. KIAA0649 (Accession NM\_014811) is another VGAM1552 host target gene. KIAA0649 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0649 BINDING SITE, designated SEQ ID:16774, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53222] Another function of VGAM1552 is therefore inhibition of KIAA0649 (Accession NM\_014811). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0649. PC2 (positive cofactor 2, multiprotein complex) Glutamine/Q-rich-associated Protein (PCQAP, Accession NM\_015889) is another VGAM1552 host target gene. PC-QAP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PCQAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCQAP BINDING SITE, designated SEQ ID:18033, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ



ID:4263.

[53223] Another function of VGAM1552 is therefore inhibition of PC2 (positive cofactor 2, multiprotein complex) Glutamine/Q-rich-associated Protein (PCQAP, Accession NM\_015889). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCQAP. Solute Carrier Family 16 (monocarboxylic acid transporters), Member 10 (SLC16A10, Accession NM\_018593) is another VGAM1552 host target gene. SLC16A10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC16A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC16A10 BINDING SITE, designated SEQ ID:20673, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53224] Another function of VGAM1552 is therefore inhibition of Solute Carrier Family 16 (monocarboxylic acid transporters), Member 10 (SLC16A10, Accession NM\_018593). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with SLC16A10. LOC125704 (Accession XM\_058931) is another VGAM1552 host target gene. LOC125704 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC125704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC125704 BINDING SITE, designated SEQ ID:36800, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53225] Another function of VGAM1552 is therefore inhibition of LOC125704 (Accession XM\_058931). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC125704. LOC134121 (Accession XM\_059692) is another VGAM1552 host target gene. LOC134121 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC134121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134121 BINDING SITE, designated SEQ ID:37064, to

the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53226] Another function of VGAM1552 is therefore inhibition of LOC134121 (Accession XM\_059692). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134121. LOC145945 (Accession XM\_096908) is another VGAM1552 host target gene. LOC145945 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145945 BINDING SITE, designated SEQ ID:40634, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53227] Another function of VGAM1552 is therefore inhibition of LOC145945 (Accession XM\_096908). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC158263 (Accession XM\_088530) is another VGAM1552 host target gene. LOC158263 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC158263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158263 BINDING SITE, designated SEQ ID:39799, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53228] Another function of VGAM1552 is therefore inhibition of LOC158263 (Accession XM\_088530). Accordingly, utilities of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158263. LOC253502 (Accession XM\_170561) is another VGAM1552 host target gene. LOC253502 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253502, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253502 BINDING SITE, designated SEQ ID:45383, to the nucleotide sequence of VGAM1552 RNA, herein designated VGAM RNA, also designated SEQ ID:4263.

[53229] Another function of VGAM1552 is therefore inhibition of LOC253502 (Accession XM\_170561). Accordingly, utilities

of VGAM1552 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253502. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1553 (VGAM1553) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53230] VGAM1553 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1553 was detected is described hereinabove with reference to Figs. 1-8.

[53231] VGAM1553 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1553 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53232] VGAM1553 gene encodes a VGAM1553 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1553 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1553 precursor RNA is designated SEQ ID:1539, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1539 is located at position 113170 relative to the genome of Macaca Mulatta Rhadinovirus.

- [53233] VGAM1553 precursor RNA folds onto itself, forming VGAM1553 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [53234] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1553 folded precursor RNA into VGAM1553 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1553 RNA is designated SEQ ID:4264, and

is provided hereinbelow with reference to the sequence listing part.

[53235] VGAM1553 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1553 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1553 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[53236] VGAM1553 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1553 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1553 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1553 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1553 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53237] The complementary binding of VGAM1553 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1553 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1553 host target RNA into VGAM1553 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53238] It is appreciated that VGAM1553 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1553 host target genes. The mRNA of each one of this plurality of VGAM1553 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–



plementary to VGAM1553 RNA, herein designated VGAM RNA, and which when bound by VGAM1553 RNA causes inhibition of translation of respective one or more VGAM1553 host target proteins.

[53239] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1553 gene, herein designated VGAM GENE, on one or more VGAM1553 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53240] It is yet further appreciated that a function of VGAM1553 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1553 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1553 correlate with, and may be deduced from, the identity of the host target genes which VGAM1553 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53241] Nucleotide sequences of the VGAM1553 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1553 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1553 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1553 are further described hereinbelow with reference to Table 1.

[53242] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1553 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1553 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53243] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1553 gene, herein designated VGAM is inhibition of expression of VGAM1553 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1553 correlate with, and may be deduced from, the identity of the target genes which VGAM1553 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53244] DKFZP564O0463 (Accession NM\_014156) is a VGAM1553 host target gene. DKFZP564O0463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O0463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0463 BINDING SITE, designated SEQ ID:15442, to the nucleotide sequence of VGAM1553 RNA, herein designated VGAM RNA, also designated SEQ ID:4264.

[53245] A function of VGAM1553 is therefore inhibition of DKFZP564O0463 (Accession NM\_014156). Accordingly, utilities of VGAM1553 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0463. KIAA0987 (Accession NM\_012307) is another VGAM1553 host target gene. KIAA0987 BIND-

ING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0987 BINDING SITE, designated SEQ ID:14675, to the nucleotide sequence of VGAM1553 RNA, herein designated VGAM RNA, also designated SEQ ID:4264.

[53246] Another function of VGAM1553 is therefore inhibition of KIAA0987 (Accession NM\_012307). Accordingly, utilities of VGAM1553 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0987. LOC116411 (Accession XM\_058095) is another VGAM1553 host target gene. LOC116411 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC116411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116411 BINDING SITE, designated SEQ ID:36571, to the nucleotide sequence of VGAM1553 RNA, herein designated VGAM RNA, also designated SEQ ID:4264.

[53247] Another function of VGAM1553 is therefore inhibition of

LOC116411 (Accession XM\_058095). Accordingly, utilities of VGAM1553 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116411. LOC90620 (Accession XM\_032986) is another VGAM1553 host target gene. LOC90620 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90620 BINDING SITE, designated SEQ ID:31806, to the nucleotide sequence of VGAM1553 RNA, herein designated VGAM RNA, also designated SEQ ID:4264.

[53248] Another function of VGAM1553 is therefore inhibition of LOC90620 (Accession XM\_032986). Accordingly, utilities of VGAM1553 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90620. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1554 (VGAM1554) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[53249] VGAM1554 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1554 was detected is described hereinabove with reference to Figs. 1–8.

[53250] VGAM1554 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1554 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53251] VGAM1554 gene encodes a VGAM1554 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1554 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1554 precursor RNA is designated SEQ ID:1540, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1540 is located at position 118520 relative to the genome of Macaca Mulatta Rhadinovirus.

[53252] VGAM1554 precursor RNA folds onto itself, forming VGAM1554 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53253] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1554 folded precursor RNA into VGAM1554 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1554 RNA is designated SEQ ID:4265, and is provided hereinbelow with reference to the sequence listing part.

[53254] VGAM1554 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1554 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1554 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[53255] VGAM1554 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1554 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1554 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1554 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1554 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR



and 5`UTR regions.

[53256] The complementary binding of VGAM1554 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1554 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1554 host target RNA into VGAM1554 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53257] It is appreciated that VGAM1554 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1554 host target genes. The mRNA of each one of this plurality of VGAM1554 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1554 RNA, herein designated VGAM RNA, and which when bound by VGAM1554 RNA causes inhibition of translation of respective one or more VGAM1554 host target proteins.

[53258] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1554 gene, herein designated VGAM GENE, on one

or more VGAM1554 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53259] It is yet further appreciated that a function of VGAM1554 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1554 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1554 correlate with, and may be deduced from, the identity of the host target genes which VGAM1554 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53260] Nucleotide sequences of the VGAM1554 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1554 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1554 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1554 are further described hereinbelow with reference to Table 1.

[53261] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1554 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1554 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53262] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1554 gene, herein designated VGAM is inhibition of expression of VGAM1554 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1554 correlate with, and may be deduced from, the identity of the target genes which VGAM1554 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53263] ATPase, Aminophospholipid Transporter-like, Class I,

Type 8A, Member 2 (ATP8A2, Accession XM\_167916) is a VGAM1554 host target gene. ATP8A2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATP8A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8A2 BINDING SITE, designated SEQ ID:44923, to the nucleotide sequence of VGAM1554 RNA, herein designated VGAM RNA, also designated SEQ ID:4265.

[53264] A function of VGAM1554 is therefore inhibition of ATPase, Aminophospholipid Transporter-like, Class I, Type 8A, Member 2 (ATP8A2, Accession XM\_167916). Accordingly, utilities of VGAM1554 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8A2. Lipin 1 (LPIN1, Accession XM\_041136) is another VGAM1554 host target gene. LPIN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LPIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPIN1 BINDING SITE, designated SEQ ID:33465, to the nucleotide se-

quence of VGAM1554 RNA, herein designated VGAM RNA, also designated SEQ ID:4265.

[53265] Another function of VGAM1554 is therefore inhibition of Lipin 1 (LPIN1, Accession XM\_041136), a gene which is involved in adipocyte differentiation (by similarity). Accordingly, utilities of VGAM1554 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPIN1. The function of LPIN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM35. Claudin 15 (CLDN15, Accession NM\_138429) is another VGAM1554 host target gene. CLDN15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLDN15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLDN15 BINDING SITE, designated SEQ ID:28793, to the nucleotide sequence of VGAM1554 RNA, herein designated VGAM RNA, also designated SEQ ID:4265.

[53266] Another function of VGAM1554 is therefore inhibition of Claudin 15 (CLDN15, Accession NM\_138429). Accordingly,

utilities of VGAM1554 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLDN15. DKFZp762K222 (Accession XM\_048721) is another VGAM1554 host target gene. DKFZp762K222 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp762K222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762K222 BINDING SITE, designated SEQ ID:35235, to the nucleotide sequence of VGAM1554 RNA, herein designated VGAM RNA, also designated SEQ ID:4265.

[53267] Another function of VGAM1554 is therefore inhibition of DKFZp762K222 (Accession XM\_048721). Accordingly, utilities of VGAM1554 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762K222. FLJ10932 (Accession NM\_018277) is another VGAM1554 host target gene. FLJ10932 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ10932 BINDING SITE, designated SEQ ID:20265, to the nucleotide sequence of VGAM1554 RNA, herein designated VGAM RNA, also designated SEQ ID:4265.

[53268] Another function of VGAM1554 is therefore inhibition of FLJ10932 (Accession NM\_018277). Accordingly, utilities of VGAM1554 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10932. FLJ23231 (Accession NM\_025079) is another VGAM1554 host target gene. FLJ23231 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23231 BINDING SITE, designated SEQ ID:24680, to the nucleotide sequence of VGAM1554 RNA, herein designated VGAM RNA, also designated SEQ ID:4265.

[53269] Another function of VGAM1554 is therefore inhibition of FLJ23231 (Accession NM\_025079). Accordingly, utilities of VGAM1554 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23231. PIG7 (Accession NM\_004862) is another

VGAM1554 host target gene. PIG7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PIG7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIG7 BINDING SITE, designated SEQ ID:11270, to the nucleotide sequence of VGAM1554 RNA, herein designated VGAM RNA, also designated SEQ ID:4265.

[53270] Another function of VGAM1554 is therefore inhibition of PIG7 (Accession NM\_004862). Accordingly, utilities of VGAM1554 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIG7. LOC152317 (Accession XM\_098189) is another VGAM1554 host target gene. LOC152317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152317 BINDING SITE, designated SEQ ID:41469, to the nucleotide sequence of VGAM1554 RNA, herein designated VGAM RNA, also designated SEQ ID:4265.



[53271] Another function of VGAM1554 is therefore inhibition of LOC152317 (Accession XM\_098189). Accordingly, utilities of VGAM1554 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152317. LOC196761 (Accession XM\_116865) is another VGAM1554 host target gene. LOC196761 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196761 BINDING SITE, designated SEQ ID:43129, to the nucleotide sequence of VGAM1554 RNA, herein designated VGAM RNA, also designated SEQ ID:4265.

[53272] Another function of VGAM1554 is therefore inhibition of LOC196761 (Accession XM\_116865). Accordingly, utilities of VGAM1554 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196761. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1555 (VGAM1555) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[53273] VGAM1555 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1555 was detected is described hereinabove with reference to Figs. 1–8.

[53274] VGAM1555 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1555 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53275] VGAM1555 gene encodes a VGAM1555 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1555 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1555 precursor RNA is designated SEQ ID:1541, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1541 is located at position 118330 relative to the genome of Macaca Mulatta Rhadinovirus.

[53276] VGAM1555 precursor RNA folds onto itself, forming VGAM1555 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53277] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1555 folded precursor RNA into VGAM1555 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 78%) nucleotide sequence of VGAM1555 RNA is designated SEQ ID:4266, and is provided hereinbelow with reference to the sequence listing part.

[53278] VGAM1555 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1555 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1555 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53279] VGAM1555 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1555 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1555 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1555 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1555 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53280] The complementary binding of VGAM1555 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1555 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1555 host target RNA into VGAM1555 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53281] It is appreciated that VGAM1555 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1555 host target genes. The mRNA of each one of this plurality of VGAM1555 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1555 RNA, herein designated VGAM RNA, and which when bound by VGAM1555 RNA causes inhibition of translation of respective one or more VGAM1555 host target proteins.

[53282] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1555 gene, herein designated VGAM GENE, on one or more VGAM1555 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53283] It is yet further appreciated that a function of VGAM1555 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1555 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1555 correlate with, and may be deduced from, the identity of the host target genes which VGAM1555 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[53284] Nucleotide sequences of the VGAM1555 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1555 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1555 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1555 are further described hereinbelow with reference to Table 1.

[53285] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1555 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1555 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53286] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1555 gene, herein designated VGAM is inhibition of expression of VGAM1555 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1555 correlate with, and may be deduced from, the identity of the target genes which VGAM1555 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53287] Colony Stimulating Factor 1 Receptor, Formerly McDonough Feline Sarcoma Viral (v-fms) Oncogene Homolog (CSF1R, Accession NM\_005211) is a VGAM1555 host target gene. CSF1R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSF1R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSF1R BINDING SITE, designated SEQ ID:11709, to the nucleotide sequence of VGAM1555 RNA, herein designated VGAM RNA, also designated SEQ ID:4266.

[53288] A function of VGAM1555 is therefore inhibition of Colony Stimulating Factor 1 Receptor, Formerly McDonough Feline Sarcoma Viral (v-fms) Oncogene Homolog (CSF1R, Accession NM\_005211), a gene which is involved in regulation of growth and differentiation of myeloid cells. Accordingly, utilities of VGAM1555 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSF1R. The function of CSF1R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM297. Neurobeachin (NBEA,



Accession XM\_170732) is another VGAM1555 host target gene. NBEA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NBEA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NBEA BINDING SITE, designated SEQ ID:45493, to the nucleotide sequence of VGAM1555 RNA, herein designated VGAM RNA, also designated SEQ ID:4266.

[53289] Another function of VGAM1555 is therefore inhibition of Neurobeachin (NBEA, Accession XM\_170732), a gene which may mediate protein-protein interactions. Accordingly, utilities of VGAM1555 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBEA. The function of NBEA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM459.EDR3 (Accession XM\_172303) is another VGAM1555 host target gene. EDR3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EDR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates

the complementarity of the nucleotide sequences of EDR3 BINDING SITE, designated SEQ ID:46068, to the nucleotide sequence of VGAM1555 RNA, herein designated VGAM RNA, also designated SEQ ID:4266.

[53290] Another function of VGAM1555 is therefore inhibition of EDR3 (Accession XM\_172303). Accordingly, utilities of VGAM1555 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDR3. FLJ14621 (Accession NM\_032811) is another VGAM1555 host target gene. FLJ14621 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14621, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14621 BINDING SITE, designated SEQ ID:26581, to the nucleotide sequence of VGAM1555 RNA, herein designated VGAM RNA, also designated SEQ ID:4266.

[53291] Another function of VGAM1555 is therefore inhibition of FLJ14621 (Accession NM\_032811). Accordingly, utilities of VGAM1555 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14621. KIAA1157 (Accession XM\_051093) is another

VGAM1555 host target gene. KIAA1157 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1157 BINDING SITE, designated SEQ ID:35753, to the nucleotide sequence of VGAM1555 RNA, herein designated VGAM RNA, also designated SEQ ID:4266.

[53292] Another function of VGAM1555 is therefore inhibition of KIAA1157 (Accession XM\_051093). Accordingly, utilities of VGAM1555 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1157. Oxysterol Binding Protein-like 6 (OSBPL6, Accession NM\_032523) is another VGAM1555 host target gene. OSBPL6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OSBPL6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL6 BINDING SITE, designated SEQ ID:26270, to the nucleotide sequence of VGAM1555 RNA, herein designated VGAM RNA, also designated SEQ

ID:4266.

[53293] Another function of VGAM1555 is therefore inhibition of Oxysterol Binding Protein-like 6 (OSBPL6, Accession NM\_032523). Accordingly, utilities of VGAM1555 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL6. LOC221583 (Accession XM\_166396) is another VGAM1555 host target gene. LOC221583 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221583, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221583 BINDING SITE, designated SEQ ID:44246, to the nucleotide sequence of VGAM1555 RNA, herein designated VGAM RNA, also designated SEQ ID:4266.

[53294] Another function of VGAM1555 is therefore inhibition of LOC221583 (Accession XM\_166396). Accordingly, utilities of VGAM1555 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221583. LOC253943 (Accession XM\_171195) is another VGAM1555 host target gene. LOC253943 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC253943, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253943 BINDING SITE, designated SEQ ID:45984, to the nucleotide sequence of VGAM1555 RNA, herein designated VGAM RNA, also designated SEQ ID:4266.

[53295] Another function of VGAM1555 is therefore inhibition of LOC253943 (Accession XM\_171195). Accordingly, utilities of VGAM1555 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253943. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1556 (VGAM1556) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53296] VGAM1556 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1556 was detected is described hereinabove with reference to Figs. 1-8.

[53297] VGAM1556 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1556 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53298] VGAM1556 gene encodes a VGAM1556 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1556 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1556 precursor RNA is designated SEQ ID:1542, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1542 is located at position 114675 relative to the genome of Macaca Mulatta Rhadinovirus.

[53299] VGAM1556 precursor RNA folds onto itself, forming VGAM1556 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53300] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1556 folded precursor RNA into VGAM1556 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1556 RNA is designated SEQ ID:4267, and is provided hereinbelow with reference to the sequence listing part.

[53301] VGAM1556 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1556 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1556 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53302] VGAM1556 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1556 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1556 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1556 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1556 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53303] The complementary binding of VGAM1556 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1556 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1556



host target RNA into VGAM1556 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53304] It is appreciated that VGAM1556 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1556 host target genes. The mRNA of each one of this plurality of VGAM1556 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1556 RNA, herein designated VGAM RNA, and which when bound by VGAM1556 RNA causes inhibition of translation of respective one or more VGAM1556 host target proteins.

[53305] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1556 gene, herein designated VGAM GENE, on one or more VGAM1556 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53306] It is yet further appreciated that a function of VGAM1556 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1556 correlate with, and may be deduced from, the identity of the host target genes which VGAM1556 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53307] Nucleotide sequences of the VGAM1556 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1556 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1556 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1556 are further

described hereinbelow with reference to Table 1.

[53308] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1556 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1556 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53309] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1556 gene, herein designated VGAM is inhibition of expression of VGAM1556 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1556 correlate with, and may be deduced from, the identity of the target genes which VGAM1556 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53310] Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM\_042963) is a VGAM1556 host target gene. ARHGEF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of ARHGEF6 BINDING SITE, designated SEQ ID:33841, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53311] A function of VGAM1556 is therefore inhibition of Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM\_042963). Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF6. Multiple Endocrine Neoplasia I (MEN1, Accession NM\_130803) is another VGAM1556 host target gene. MEN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MEN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEN1 BINDING SITE, designated SEQ ID:28295, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53312] Another function of VGAM1556 is therefore inhibition of Multiple Endocrine Neoplasia I (MEN1, Accession NM\_130803). Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with MEN1. Myosin X (MYO10, Accession NM\_012334) is another VGAM1556 host target gene. MYO10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MYO10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO10 BINDING SITE, designated SEQ ID:14728, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53313] Another function of VGAM1556 is therefore inhibition of Myosin X (MYO10, Accession NM\_012334), a gene which is an unconventional myosin. Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO10. The function of MYO10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. Bromodomain Containing 4 (BRD4, Accession NM\_058243) is another VGAM1556 host target gene. BRD4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BRD4,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRD4 BINDING SITE, designated SEQ ID:27777, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53314] Another function of VGAM1556 is therefore inhibition of Bromodomain Containing 4 (BRD4, Accession NM\_058243). Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRD4. FLJ10415 (Accession NM\_018089) is another VGAM1556 host target gene. FLJ10415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10415 BINDING SITE, designated SEQ ID:19852, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53315] Another function of VGAM1556 is therefore inhibition of FLJ10415 (Accession NM\_018089). Accordingly, utilities of

VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10415. FLJ12768 (Accession NM\_025163) is another VGAM1556 host target gene. FLJ12768 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12768, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12768 BINDING SITE, designated SEQ ID:24802, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53316] Another function of VGAM1556 is therefore inhibition of FLJ12768 (Accession NM\_025163). Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12768. ISL2 Transcription Factor, LIM/homeodomain, (islet-2) (ISL2, Accession XM\_047951) is another VGAM1556 host target gene. ISL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ISL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of ISL2 BINDING SITE, designated SEQ ID:35079, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53317] Another function of VGAM1556 is therefore inhibition of ISL2 Transcription Factor, LIM/homeodomain, (islet-2) (ISL2, Accession XM\_047951). Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ISL2. PDEF (Accession NM\_012391) is another VGAM1556 host target gene. PDEF BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PDEF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDEF BINDING SITE, designated SEQ ID:14745, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53318] Another function of VGAM1556 is therefore inhibition of PDEF (Accession NM\_012391). Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDEF.



SCYB11 (Accession XM\_113426) is another VGAM1556 host target gene. SCYB11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCYB11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYB11 BINDING SITE, designated SEQ ID:42258, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53319] Another function of VGAM1556 is therefore inhibition of SCYB11 (Accession XM\_113426). Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCYB11. LOC147299 (Accession XM\_085763) is another VGAM1556 host target gene. LOC147299 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147299 BINDING SITE, designated SEQ ID:38328, to the nucleotide sequence of VGAM1556 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4267.

[53320] Another function of VGAM1556 is therefore inhibition of LOC147299 (Accession XM\_085763). Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147299. LOC93268 (Accession XM\_050158) is another VGAM1556 host target gene. LOC93268 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93268 BINDING SITE, designated SEQ ID:35585, to the nucleotide sequence of VGAM1556 RNA, herein designated VGAM RNA, also designated SEQ ID:4267.

[53321] Another function of VGAM1556 is therefore inhibition of LOC93268 (Accession XM\_050158). Accordingly, utilities of VGAM1556 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93268. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1557 (VGAM1557) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53322] VGAM1557 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1557 was detected is described hereinabove with reference to Figs. 1–8.

[53323] VGAM1557 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1557 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53324] VGAM1557 gene encodes a VGAM1557 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1557 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1557 precursor RNA is designated SEQ ID:1543, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1543 is located at position 114790 relative to the genome of Macaca Mulatta Rhadinovirus.

[53325] VGAM1557 precursor RNA folds onto itself, forming

VGAM1557 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53326] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1557 folded precursor RNA into VGAM1557 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1557 RNA is designated SEQ ID:4268, and is provided hereinbelow with reference to the sequence listing part.

[53327] VGAM1557 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1557 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1557 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53328] VGAM1557 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1557 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1557 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1557 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1557 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53329] The complementary binding of VGAM1557 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1557 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1557 host target RNA into VGAM1557 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53330] It is appreciated that VGAM1557 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1557 host target genes. The mRNA of each one of this plurality of VGAM1557 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1557 RNA, herein designated VGAM RNA, and which when bound by VGAM1557 RNA causes inhibition of translation of respective one or more VGAM1557 host target proteins.

[53331] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1557 gene, herein designated VGAM GENE, on one or more VGAM1557 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53332] It is yet further appreciated that a function of VGAM1557 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1557 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1557 correlate with, and may be deduced from, the identity of the host target genes which VGAM1557 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53333] Nucleotide sequences of the VGAM1557 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1557 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1557 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1557 are further described hereinbelow with reference to Table 1.

[53334] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1557 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1557 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53335] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1557 gene, herein designated VGAM is inhibition of expression of VGAM1557 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1557 correlate with, and may be deduced from, the identity of the target genes which VGAM1557 binds and inhibits, and the function of these target genes,



as elaborated hereinbelow.

[53336] Enabled Homolog (Drosophila) (ENAH, Accession NM\_018212) is a VGAM1557 host target gene. ENAH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENAH BINDING SITE, designated SEQ ID:20124, to the nucleotide sequence of VGAM1557 RNA, herein designated VGAM RNA, also designated SEQ ID:4268.

[53337] A function of VGAM1557 is therefore inhibition of Enabled Homolog (Drosophila) (ENAH, Accession NM\_018212). Accordingly, utilities of VGAM1557 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENAH. FLJ12484 (Accession NM\_022767) is another VGAM1557 host target gene. FLJ12484 BINDING SITE1 and FLJ12484 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ12484, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12484 BINDING SITE1 and

FLJ12484 BINDING SITE2, designated SEQ ID:23024 and SEQ ID:34522 respectively, to the nucleotide sequence of VGAM1557 RNA, herein designated VGAM RNA, also designated SEQ ID:4268.

[53338] Another function of VGAM1557 is therefore inhibition of FLJ12484 (Accession NM\_022767). Accordingly, utilities of VGAM1557 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12484. Zinc Finger Protein 185 (LIM domain) (ZNF185, Accession NM\_007150) is another VGAM1557 host target gene. ZNF185 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF185, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF185 BINDING SITE, designated SEQ ID:14002, to the nucleotide sequence of VGAM1557 RNA, herein designated VGAM RNA, also designated SEQ ID:4268.

[53339] Another function of VGAM1557 is therefore inhibition of Zinc Finger Protein 185 (LIM domain) (ZNF185, Accession NM\_007150). Accordingly, utilities of VGAM1557 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with ZNF185. LOC145828 (Accession XM\_096879) is another VGAM1557 host target gene. LOC145828 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145828 BINDING SITE, designated SEQ ID:40612, to the nucleotide sequence of VGAM1557 RNA, herein designated VGAM RNA, also designated SEQ ID:4268.

[53340] Another function of VGAM1557 is therefore inhibition of LOC145828 (Accession XM\_096879). Accordingly, utilities of VGAM1557 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145828. LOC152926 (Accession XM\_087562) is another VGAM1557 host target gene. LOC152926 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152926, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152926 BINDING SITE, designated SEQ ID:39340, to

the nucleotide sequence of VGAM1557 RNA, herein designated VGAM RNA, also designated SEQ ID:4268.

[53341] Another function of VGAM1557 is therefore inhibition of LOC152926 (Accession XM\_087562). Accordingly, utilities of VGAM1557 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152926. LOC220662 (Accession XM\_165978) is another VGAM1557 host target gene. LOC220662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220662 BINDING SITE, designated SEQ ID:43824, to the nucleotide sequence of VGAM1557 RNA, herein designated VGAM RNA, also designated SEQ ID:4268.

[53342] Another function of VGAM1557 is therefore inhibition of LOC220662 (Accession XM\_165978). Accordingly, utilities of VGAM1557 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220662. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1558 (VGAM1558) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53343] VGAM1558 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1558 was detected is described hereinabove with reference to Figs. 1–8.

[53344] VGAM1558 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Virus. VGAM1558 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53345] VGAM1558 gene encodes a VGAM1558 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1558 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1558 precursor RNA is designated SEQ ID:1544, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1544 is located at position 8996 relative to the genome of Bean Common Mosaic Virus.

[53346] VGAM1558 precursor RNA folds onto itself, forming VGAM1558 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53347] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1558 folded precursor RNA into VGAM1558 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1558 RNA is designated SEQ ID:4269, and is provided hereinbelow with reference to the sequence listing part.

[53348] VGAM1558 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1558 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1558 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53349] VGAM1558 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1558 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1558 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1558 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1558 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53350] The complementary binding of VGAM1558 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1558 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1558 host target RNA into VGAM1558 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53351] It is appreciated that VGAM1558 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1558 host target genes. The mRNA of each one of this plurality of VGAM1558 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1558 RNA, herein designated VGAM RNA, and which when bound by VGAM1558 RNA causes inhibition of translation of respective one or more VGAM1558 host target proteins.

[53352] It is further appreciated by one skilled in the art that the



mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1558 gene, herein designated VGAM GENE, on one or more VGAM1558 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53353] It is yet further appreciated that a function of VGAM1558 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1558 correlate with, and may be deduced from, the

identity of the host target genes which VGAM1558 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53354] Nucleotide sequences of the VGAM1558 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1558 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1558 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1558 are further described hereinbelow with reference to Table 1.

[53355] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1558 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1558 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53356] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1558 gene, herein designated VGAM is inhibition of expression of VGAM1558 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1558 correlate with, and may be deduced from, the identity of the target genes which VGAM1558

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53357] Ceroid–lipofuscinosis, Neuronal 6, Late Infantile, Variant (CLN6, Accession NM\_017882) is a VGAM1558 host target gene. CLN6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLN6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN6 BINDING SITE, designated SEQ ID:19549, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53358] A function of VGAM1558 is therefore inhibition of Ceroid–lipofuscinosis, Neuronal 6, Late Infantile, Variant (CLN6, Accession NM\_017882). Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN6. Ectodermal–neural Cortex (with BTB–like domain) (ENC1, Accession NM\_003633) is another VGAM1558 host target gene. ENC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ENC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta–

ble 2 illustrates the complementarity of the nucleotide sequences of ENC1 BINDING SITE, designated SEQ ID:9696, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53359] Another function of VGAM1558 is therefore inhibition of Ectodermal–neural Cortex (with BTB–like domain) (ENC1, Accession NM\_003633), a gene which is an actin–binding protein involved in the regulation of neuronal process formation and in differentiation of neural crest cells. Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENC1. The function of ENC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM233.Procollagen–lysine, 2–oxoglutarate 5–dioxygenase (lysine hydroxylase, Ehlers–Danlos syndrome type VI) (PLOD, Accession NM\_000302) is another VGAM1558 host target gene. PLOD BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PLOD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se–

quences of PLOD BINDING SITE, designated SEQ ID:5843, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53360] Another function of VGAM1558 is therefore inhibition of Procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI) (PLOD, Accession NM\_000302). Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLOD. Pyrroline-5-carboxylate Synthetase (glutamate gamma-semialdehyde synthetase) (PYCS, Accession NM\_002860) is another VGAM1558 host target gene. PYCS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PYCS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYCS BINDING SITE, designated SEQ ID:8760, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53361] Another function of VGAM1558 is therefore inhibition of Pyrroline-5-carboxylate Synthetase (glutamate gamma-semialdehyde synthetase) (PYCS, Accession NM\_002860).

Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYCS. CASPR3 (Accession NM\_024879) is another VGAM1558 host target gene. CASPR3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CASPR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASPR3 BINDING SITE, designated SEQ ID:24315, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53362] Another function of VGAM1558 is therefore inhibition of CASPR3 (Accession NM\_024879). Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASPR3. KIAA1040 (Accession XM\_051091) is another VGAM1558 host target gene. KIAA1040 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1040 BINDING SITE, designated SEQ ID:35745, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53363] Another function of VGAM1558 is therefore inhibition of KIAA1040 (Accession XM\_051091). Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1040. KIAA1764 (Accession XM\_045086) is another VGAM1558 host target gene. KIAA1764 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1764, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1764 BINDING SITE, designated SEQ ID:34352, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53364] Another function of VGAM1558 is therefore inhibition of KIAA1764 (Accession XM\_045086). Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1764. KIAA1854 (Accession XM\_049884) is another

VGAM1558 host target gene. KIAA1854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35529, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53365] Another function of VGAM1558 is therefore inhibition of KIAA1854 (Accession XM\_049884). Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. LOC200197 (Accession XM\_114148) is another VGAM1558 host target gene. LOC200197 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200197 BINDING SITE, designated SEQ ID:42729, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.



[53366] Another function of VGAM1558 is therefore inhibition of LOC200197 (Accession XM\_114148). Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200197. LOC203232 (Accession XM\_049274) is another VGAM1558 host target gene. LOC203232 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203232 BINDING SITE, designated SEQ ID:35373, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53367] Another function of VGAM1558 is therefore inhibition of LOC203232 (Accession XM\_049274). Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203232. LOC90233 (Accession NM\_138347) is another VGAM1558 host target gene. LOC90233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90233, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90233 BINDING SITE, designated SEQ ID:28742, to the nucleotide sequence of VGAM1558 RNA, herein designated VGAM RNA, also designated SEQ ID:4269.

[53368] Another function of VGAM1558 is therefore inhibition of LOC90233 (Accession NM\_138347). Accordingly, utilities of VGAM1558 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90233. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1559 (VGAM1559) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53369] VGAM1559 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1559 was detected is described hereinabove with reference to Figs. 1–8.

[53370] VGAM1559 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Virus. VGAM1559 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53371] VGAM1559 gene encodes a VGAM1559 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1559 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1559 precursor RNA is designated SEQ ID:1545, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1545 is located at position 3572 relative to the genome of Bean Common Mosaic Virus.

[53372] VGAM1559 precursor RNA folds onto itself, forming VGAM1559 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53373] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1559 folded precursor RNA into VGAM1559

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1559 RNA is designated SEQ ID:4270, and is provided hereinbelow with reference to the sequence listing part.

[53374] VGAM1559 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1559 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1559 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53375] VGAM1559 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1559 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1559 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1559 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1559 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53376] The complementary binding of VGAM1559 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1559 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1559 host target RNA into VGAM1559 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[53377] It is appreciated that VGAM1559 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1559 host target genes. The mRNA of each one of this plurality of VGAM1559 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1559 RNA, herein designated VGAM RNA, and which when bound by VGAM1559 RNA causes inhibition of translation of respective one or more VGAM1559 host target proteins.

[53378] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1559 gene, herein designated VGAM GENE, on one or more VGAM1559 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53379] It is yet further appreciated that a function of VGAM1559 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1559 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1559 correlate with, and may be deduced from, the identity of the host target genes which VGAM1559 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53380] Nucleotide sequences of the VGAM1559 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1559 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1559 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1559 are further described hereinbelow with reference to Table 1.

[53381] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1559 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1559 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53382] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1559 gene, herein designated VGAM is inhibition of expression of VGAM1559 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1559 correlate with, and may be deduced from, the identity of the target genes which VGAM1559 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53383] Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 3 (GNAI3, Accession NM\_006496) is a VGAM1559 host target gene. GNAI3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAI3 BINDING SITE, designated SEQ ID:13239, to the



nucleotide sequence of VGAM1559 RNA, herein designated VGAM RNA, also designated SEQ ID:4270.

[53384] A function of VGAM1559 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 3 (GNAI3, Accession NM\_006496), a gene which stimulates receptor regulated K<sup>+</sup>-channels. Accordingly, utilities of VGAM1559 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAI3. The function of GNAI3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM45.Chondrolectin (CHODL, Accession NM\_024944) is another VGAM1559 host target gene. CHODL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHODL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHODL BINDING SITE, designated SEQ ID:24489, to the nucleotide sequence of VGAM1559 RNA, herein designated VGAM RNA, also designated SEQ ID:4270.

[53385] Another function of VGAM1559 is therefore inhibition of

Chondrolectin (CHODL, Accession NM\_024944). Accordingly, utilities of VGAM1559 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHODL. KIAA0416 (Accession NM\_015564) is another VGAM1559 host target gene. KIAA0416 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0416 BINDING SITE, designated SEQ ID:17832, to the nucleotide sequence of VGAM1559 RNA, herein designated VGAM RNA, also designated SEQ ID:4270.

[53386] Another function of VGAM1559 is therefore inhibition of KIAA0416 (Accession NM\_015564). Accordingly, utilities of VGAM1559 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0416. LOC145951 (Accession XM\_085283) is another VGAM1559 host target gene. LOC145951 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145951, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC145951 BINDING SITE, designated SEQ ID:38016, to the nucleotide sequence of VGAM1559 RNA, herein designated VGAM RNA, also designated SEQ ID:4270.

[53387] Another function of VGAM1559 is therefore inhibition of LOC145951 (Accession XM\_085283). Accordingly, utilities of VGAM1559 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145951. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1560 (VGAM1560) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53388] VGAM1560 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1560 was detected is described hereinabove with reference to Figs. 1–8.

[53389] VGAM1560 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Virus. VGAM1560 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[53390] VGAM1560 gene encodes a VGAM1560 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1560 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1560 precursor RNA is designated SEQ ID:1546, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1546 is located at position 6352 relative to the genome of Bean Common Mosaic Virus.

[53391] VGAM1560 precursor RNA folds onto itself, forming VGAM1560 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53392] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1560 folded precursor RNA into VGAM1560 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1560 RNA is designated SEQ ID:4271, and is provided hereinbelow with reference to the sequence listing part.

[53393] VGAM1560 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1560 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1560 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53394] VGAM1560 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1560 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1560 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1560 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1560 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53395] The complementary binding of VGAM1560 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1560 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1560 host target RNA into VGAM1560 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53396] It is appreciated that VGAM1560 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1560 host target genes. The mRNA of each one of this plurality of VGAM1560 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1560 RNA, herein designated VGAM RNA, and which when bound by VGAM1560 RNA causes inhibition of translation of respective one or more VGAM1560 host target proteins.

[53397] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1560 gene, herein designated VGAM GENE, on one or more VGAM1560 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53398] It is yet further appreciated that a function of VGAM1560 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1560 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1560 correlate with, and may be deduced from, the identity of the host target genes which VGAM1560 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53399] Nucleotide sequences of the VGAM1560 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1560 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1560 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1560 are further described hereinbelow with reference to Table 1.

[53400] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of



Fig. 1, found on VGAM1560 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1560 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53401] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1560 gene, herein designated VGAM is inhibition of expression of VGAM1560 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1560 correlate with, and may be deduced from, the identity of the target genes which VGAM1560 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53402] EPB72 (Accession NM\_004099) is a VGAM1560 host target gene. EPB72 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPB72, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB72 BINDING SITE, designated SEQ ID:10303, to the nucleotide sequence of VGAM1560 RNA, herein designated VGAM RNA, also designated SEQ ID:4271.

[53403] A function of VGAM1560 is therefore inhibition of EPB72 (Accession NM\_004099), a gene which may regulate cation conductance. Accordingly, utilities of VGAM1560 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB72. The function of EPB72 has been established by previous studies. Erythrocyte surface protein band 7.2 is a 29,000-kD integral membrane protein that is exposed on the cytoplasmic surface of the membrane and is susceptible to phosphorylation by a cAMP-dependent protein kinase. Deficiency of this protein in red cells is responsible for stomatocytosis (OMIM Ref. No. 185000). The same protein can be demonstrated in human cell lines of epithelial and lymphoid origin, notably in HeLa cells. Hiebl-Dirschmied et al. (1991), therefore, could screen HeLa cell cDNA expression libraries with antibodies to the protein in order to isolate cDNA clones, determine the nucleotide sequence, and study the structure of the protein. HeLa and bone marrow cell-derived sequences were identical, except for one nucleotide; the deduced sequence of 287 amino acids was confirmed by sequence identity with peptides of the erythroid protein. Structural analysis assigned band 7 protein to the type Ib transmembrane proteins. Westberg et al.

(1993) used a cDNA clone coding for stomatin to determine the chromosomal localization of the EPB72 gene. They assigned the gene to human chromosome 9 by Southern blot analysis of somatic cell hybrids. By analysis of hybrid cells containing only parts of chromosome 9, they regionalized the assignment to 9q34.1, proximal to the breakpoint that creates the Philadelphia chromosome of chronic myeloid leukemia (CML; 151410) and, therefore, proximal to the Abelson oncogene (OMIM Ref. No. 189980). Using fluorescence in situ hybridization, Gallagher et al. (1993) likewise mapped the EPB72 gene to 9q33–q34. They showed that EPB72 was not translocated with the 3–prime end of the ABL gene in the Philadelphia chromosome, suggesting that the EPB72 gene is centromeric to the ABL gene. Pilz et al. (1994) demonstrated that the homologous gene is located on mouse chromosome 2. To gain additional insight into the structure and function of this protein, Gallagher et al. (1995) cloned the mouse band 7.2b cDNA and studied its tissue-specific expression. They isolated 2,873 bp of cDNA with an open reading frame of 852 bp. The predicted protein was 284 amino acids with a molecular weight of 31 kD. They detected a wide pattern of expression, with high levels of

mRNA in heart, liver, skeletal muscle, and testis but low levels in lung, brain, and spleen. Using fluorescence in situ hybridization, the murine band 7.2b gene was mapped to chromosome 2, at the border of the distal region of 2B and proximal region of C1, syntenic to 9q, the location of the human homolog. Models of the predicted protein structure showed a short NH<sub>2</sub>-terminal head, a strongly hydrophobic 28-amino acid stretch presumably encoding a single membrane-spanning domain, and a large domain composed of beta sheet and alpha helix. Database searching showed no significant homology of other known proteins to either the human or the murine band 7.2b. Gallagher and Forget (1995) determined the sequence of the full-length human band 7.2b cDNA, characterized the genomic structure of the EPB72 gene, studied its pattern of expression in different tissues, and characterized the promoter of the gene. The gene is composed of 7 exons distributed over 40 kb of DNA. Its promoter was identified as lacking a TATA box and to be GC-rich. It directed high-level expression of a reporter gene in both erythroid and non-erythroid cells. Unfried et al. (1995) showed that the human EPB72 gene contains 7 exons spanning about 30 kb. Two polyadenylation signals

were found in the 3-prime UTR accounting for the 3.2- and 3.3-kb RNAs that are observed in Northern blots. Animal model experiments lend further support to the function of EPB72. To examine the relationship between erythrocyte membrane protein 7.2b deficiency and the hemolytic anemia of human hereditary stomatocytosis, Zhu et al. (1999) created 7.2b knockout mice by standard gene targeting approaches. Despite a complete absence of protein 7.2b in homozygous knockout mice, there was no hemolytic anemia, and mouse red blood cells were normal in morphology, cell indices, hydration status, monovalent cation content, and ability to translocate lipids. Thus, their experiments suggested that 7.2b deficiency plays no direct role in the etiology of stomatocytosis and excluded any role of this protein as a mediator of cation transport in red blood cells.

[53404] It is appreciated that the abovementioned animal model for EPB72 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[53405] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53406] Zhu, Y.; Paszty, C.; Turetsky, T.; Tsai, S.; Kuypers, F. A.; Lee, G.; Cooper, P.; Gallagher, P. G.; Stevens, M. E.; Rubin, E.; Mohandas, N.; Mentzer, W. C. : Stomatocytosis is absent in 'stomatin'-deficient murine red blood cells. Blood 93: 2404–2410, 1999. ; and

[53407] Zhu, Y.; Paszty, C.; Turetsky, T.; Tsai, S.; Kuypers, F. A.; Lee, G.; Cooper, P.; Gallagher, P. G.; Stevens, M. E.; Rubin, E.; Mohandas, N.; Mentzer, W. C. : Stomatocytosis is absent in.

[53408] Further studies establishing the function and utilities of EPB72 are found in John Hopkins OMIM database record ID 133090, and in cited publications numbered 4369–4376 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hyaluronan-mediated Motility Receptor (RHAMM) (HMMR, Accession NM\_012484) is another VGAM1560 host target gene. HMMR BINDING SITE1 and HMMR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HMMR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMMR BINDING SITE1 and HMMR BINDING SITE2, design-

nated SEQ ID:14861 and SEQ ID:14863 respectively, to the nucleotide sequence of VGAM1560 RNA, herein designated VGAM RNA, also designated SEQ ID:4271.

[53409] Another function of VGAM1560 is therefore inhibition of Hyaluronan-mediated Motility Receptor (RHAMM) (HMMR, Accession NM\_012484). Accordingly, utilities of VGAM1560 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMMR. KIAA0354 (Accession NM\_014872) is another VGAM1560 host target gene. KIAA0354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0354 BINDING SITE, designated SEQ ID:16995, to the nucleotide sequence of VGAM1560 RNA, herein designated VGAM RNA, also designated SEQ ID:4271.

[53410] Another function of VGAM1560 is therefore inhibition of KIAA0354 (Accession NM\_014872). Accordingly, utilities of VGAM1560 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0354. LOC144308 (Accession XM\_096575) is another

VGAM1560 host target gene. LOC144308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144308 BINDING SITE, designated SEQ ID:40403, to the nucleotide sequence of VGAM1560 RNA, herein designated VGAM RNA, also designated SEQ ID:4271.

[53411] Another function of VGAM1560 is therefore inhibition of LOC144308 (Accession XM\_096575). Accordingly, utilities of VGAM1560 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144308. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1561 (VGAM1561) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53412] VGAM1561 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1561 was detected is de-



scribed hereinabove with reference to Figs. 1–8.

[53413] VGAM1561 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Virus. VGAM1561 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53414] VGAM1561 gene encodes a VGAM1561 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1561 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1561 precursor RNA is designated SEQ ID:1547, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1547 is located at position 7254 relative to the genome of Bean Common Mosaic Virus.

[53415] VGAM1561 precursor RNA folds onto itself, forming VGAM1561 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53416] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1561 folded precursor RNA into VGAM1561 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1561 RNA is designated SEQ ID:4272, and is provided hereinbelow with reference to the sequence listing part.

[53417] VGAM1561 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1561 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1561 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53418] VGAM1561 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1561 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1561 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1561 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1561 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53419] The complementary binding of VGAM1561 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1561 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1561 host target RNA into VGAM1561 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53420] It is appreciated that VGAM1561 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1561 host target genes. The mRNA of each one of this plurality of VGAM1561 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1561 RNA, herein designated VGAM RNA, and which when bound by VGAM1561 RNA causes inhibition of translation of respective one or more VGAM1561 host target proteins.

[53421] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1561 gene, herein designated VGAM GENE, on one or more VGAM1561 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53422] It is yet further appreciated that a function of VGAM1561 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1561 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1561 correlate with, and may be deduced from, the identity of the host target genes which VGAM1561 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53423] Nucleotide sequences of the VGAM1561 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1561 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1561 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1561 are further described hereinbelow with reference to Table 1.

[53424] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1561 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1561 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53425] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1561 gene, herein designated VGAM is inhibition of expression of VGAM1561 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1561 correlate with, and may be deduced from, the identity of the target genes which VGAM1561 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53426] KIAA0872 (Accession NM\_014940) is a VGAM1561 host target gene. KIAA0872 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0872 BINDING SITE, designated SEQ ID:17243, to the nucleotide sequence of VGAM1561 RNA, herein designated VGAM RNA, also designated SEQ ID:4272.

[53427] A function of VGAM1561 is therefore inhibition of KIAA0872 (Accession NM\_014940). Accordingly, utilities of VGAM1561 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0872. LOC219445 (Accession XM\_166212) is another VGAM1561 host target gene. LOC219445 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219445 BINDING SITE, designated SEQ ID:44011, to the nucleotide sequence of VGAM1561 RNA, herein designated VGAM RNA, also designated SEQ ID:4272.

[53428] Another function of VGAM1561 is therefore inhibition of LOC219445 (Accession XM\_166212). Accordingly, utilities of VGAM1561 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC219445. LOC58525 (Accession XM\_086045) is another VGAM1561 host target gene. LOC58525 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC58525, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58525 BINDING SITE, designated SEQ ID:38455, to the nucleotide sequence of VGAM1561 RNA, herein designated VGAM RNA, also designated SEQ ID:4272.

[53429] Another function of VGAM1561 is therefore inhibition of LOC58525 (Accession XM\_086045). Accordingly, utilities of VGAM1561 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58525. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1562 (VGAM1562) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53430] VGAM1562 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.



The method by which VGAM1562 was detected is described hereinabove with reference to Figs. 1–8.

[53431] VGAM1562 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Virus. VGAM1562 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53432] VGAM1562 gene encodes a VGAM1562 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1562 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1562 precursor RNA is designated SEQ ID:1548, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1548 is located at position 2292 relative to the genome of Bean Common Mosaic Virus.

[53433] VGAM1562 precursor RNA folds onto itself, forming VGAM1562 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53434] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1562 folded precursor RNA into VGAM1562 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1562 RNA is designated SEQ ID:4273, and is provided hereinbelow with reference to the sequence listing part.

[53435] VGAM1562 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1562 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1562 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53436] VGAM1562 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1562 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1562 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1562 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1562 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[53437] The complementary binding of VGAM1562 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1562 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1562 host target RNA into VGAM1562 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53438] It is appreciated that VGAM1562 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1562 host target genes. The mRNA of each one of this plurality of VGAM1562 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1562 RNA, herein designated VGAM RNA, and which when bound by VGAM1562 RNA causes inhibition of translation of respective one or more VGAM1562 host target proteins.

[53439] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1562 gene, herein designated VGAM GENE, on one or more VGAM1562 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53440] It is yet further appreciated that a function of VGAM1562 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1562 correlate with, and may be deduced from, the identity of the host target genes which VGAM1562 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53441] Nucleotide sequences of the VGAM1562 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1562 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1562 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1562 are further described hereinbelow with reference to Table 1.

[53442] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1562 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1562 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53443] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1562 gene, herein designated VGAM is inhibition of expression of VGAM1562 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1562 correlate with, and may be deduced from, the identity of the target genes which VGAM1562 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53444] Chemokine (C-C motif) Receptor-like 1 (CCRL1, Accession NM\_016557) is a VGAM1562 host target gene. CCRL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCRL1, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCRL1 BINDING SITE, designated SEQ ID:18630, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53445] A function of VGAM1562 is therefore inhibition of Chemokine (C-C motif) Receptor-like 1 (CCRL1, Accession NM\_016557), a gene which is a G protein-coupled receptor that binds chemokines of the CC subfamily, especially MCP-4, ELC (SCYA19) and TECK (SCYA25). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCRL1. The function of CCRL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM546. Solute Carrier Family 26, Member 4 (SLC26A4, Accession NM\_000441) is another VGAM1562 host target gene. SLC26A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC26A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of SLC26A4 BINDING SITE, designated SEQ ID:6027, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53446] Another function of VGAM1562 is therefore inhibition of Solute Carrier Family 26, Member 4 (SLC26A4, Accession NM\_000441). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A4. ALK7 (Accession XM\_065712) is another VGAM1562 host target gene. ALK7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALK7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALK7 BINDING SITE, designated SEQ ID:37296, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53447] Another function of VGAM1562 is therefore inhibition of ALK7 (Accession XM\_065712). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALK7. DKFZp761F2014 (Accession NM\_020215) is another



VGAM1562 host target gene. DKFZp761F2014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761F2014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761F2014 BINDING SITE, designated SEQ ID:21458, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53448] Another function of VGAM1562 is therefore inhibition of DKFZp761F2014 (Accession NM\_020215). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761F2014. F-box Only Protein 4 (FBXO4, Accession NM\_033484) is another VGAM1562 host target gene. FBXO4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO4 BINDING SITE, designated SEQ ID:27261, to the nucleotide sequence of VGAM1562 RNA,

herein designated VGAM RNA, also designated SEQ ID:4273.

[53449] Another function of VGAM1562 is therefore inhibition of F-box Only Protein 4 (FBXO4, Accession NM\_033484). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO4. FLJ10619 (Accession NM\_018156) is another VGAM1562 host target gene. FLJ10619 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10619 BINDING SITE, designated SEQ ID:19967, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53450] Another function of VGAM1562 is therefore inhibition of FLJ10619 (Accession NM\_018156). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10619. FLJ11210 (Accession XM\_005298) is another VGAM1562 host target gene. FLJ11210 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ11210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11210 BINDING SITE, designated SEQ ID:29974, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53451] Another function of VGAM1562 is therefore inhibition of FLJ11210 (Accession XM\_005298). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11210. FLJ12619 (Accession NM\_030939) is another VGAM1562 host target gene. FLJ12619 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12619 BINDING SITE, designated SEQ ID:25210, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53452] Another function of VGAM1562 is therefore inhibition of FLJ12619 (Accession NM\_030939). Accordingly, utilities of

VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12619. FLJ20086 (Accession NM\_017661) is another VGAM1562 host target gene. FLJ20086 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20086, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20086 BINDING SITE, designated SEQ ID:19187, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53453] Another function of VGAM1562 is therefore inhibition of FLJ20086 (Accession NM\_017661). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20086. FLJ21916 (Accession NM\_023112) is another VGAM1562 host target gene. FLJ21916 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21916

BINDING SITE, designated SEQ ID:23385, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53454] Another function of VGAM1562 is therefore inhibition of FLJ21916 (Accession NM\_023112). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21916. FLJ23511 (Accession NM\_032239) is another VGAM1562 host target gene. FLJ23511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23511 BINDING SITE, designated SEQ ID:25962, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53455] Another function of VGAM1562 is therefore inhibition of FLJ23511 (Accession NM\_032239). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23511. HSAJ1454 (Accession NM\_016950) is another VGAM1562 host target gene. HSAJ1454 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSAJ1454, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSAJ1454 BINDING SITE, designated SEQ ID:18866, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53456] Another function of VGAM1562 is therefore inhibition of HSAJ1454 (Accession NM\_016950). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSAJ1454. KIAA0992 (Accession NM\_016081) is another VGAM1562 host target gene. KIAA0992 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0992 BINDING SITE, designated SEQ ID:18156, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53457] Another function of VGAM1562 is therefore inhibition of

KIAA0992 (Accession NM\_016081). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0992. KIAA1323 (Accession XM\_032146) is another VGAM1562 host target gene. KIAA1323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1323 BINDING SITE, designated SEQ ID:31562, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53458] Another function of VGAM1562 is therefore inhibition of KIAA1323 (Accession XM\_032146). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1323. Ras Protein-specific Guanine Nucleotide-releasing Factor 2 (RASGRF2, Accession XM\_027943) is another VGAM1562 host target gene. RASGRF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASGRF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASGRF2 BINDING SITE, designated SEQ ID:30597, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53459] Another function of VGAM1562 is therefore inhibition of Ras Protein-specific Guanine Nucleotide-releasing Factor 2 (RASGRF2, Accession XM\_027943). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASGRF2. SAM Domain, SH3 Domain and Nuclear Localisation Signals, 1 (SAMSN1, Accession NM\_022136) is another VGAM1562 host target gene. SAMSN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SAMSN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SAMSN1 BINDING SITE, designated SEQ ID:22696, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53460] Another function of VGAM1562 is therefore inhibition of SAM Domain, SH3 Domain and Nuclear Localisation Sig-



nals, 1 (SAMSN1, Accession NM\_022136). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAMSN1. STIP-1 (Accession XM\_045694) is another VGAM1562 host target gene. STIP-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STIP-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STIP-1 BINDING SITE, designated SEQ ID:34526, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53461] Another function of VGAM1562 is therefore inhibition of STIP-1 (Accession XM\_045694). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STIP-1. TA-KRP (Accession NM\_032505) is another VGAM1562 host target gene. TA-KRP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TA-KRP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of TA-KRP BINDING SITE, designated SEQ ID:26252, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53462] Another function of VGAM1562 is therefore inhibition of TA-KRP (Accession NM\_032505). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TA-KRP. T-cell Lymphoma Invasion and Metastasis 2 (TIAM2, Accession NM\_012454) is another VGAM1562 host target gene. TIAM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIAM2 BINDING SITE, designated SEQ ID:14822, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53463] Another function of VGAM1562 is therefore inhibition of T-cell Lymphoma Invasion and Metastasis 2 (TIAM2, Accession NM\_012454). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with TIAM2. LOC150605 (Accession XM\_097927) is another VGAM1562 host target gene. LOC150605 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150605, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150605 BINDING SITE, designated SEQ ID:41228, to the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53464] Another function of VGAM1562 is therefore inhibition of LOC150605 (Accession XM\_097927). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150605. LOC152756 (Accession XM\_098262) is another VGAM1562 host target gene. LOC152756 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152756, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152756 BINDING SITE, designated SEQ ID:41549, to

the nucleotide sequence of VGAM1562 RNA, herein designated VGAM RNA, also designated SEQ ID:4273.

[53465] Another function of VGAM1562 is therefore inhibition of LOC152756 (Accession XM\_098262). Accordingly, utilities of VGAM1562 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152756. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1563 (VGAM1563) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53466] VGAM1563 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1563 was detected is described hereinabove with reference to Figs. 1–8.

[53467] VGAM1563 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Virus. VGAM1563 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53468] VGAM1563 gene encodes a VGAM1563 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1563 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1563 precursor RNA is designated SEQ ID:1549, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1549 is located at position 9514 relative to the genome of Bean Common Mosaic Virus.

[53469] VGAM1563 precursor RNA folds onto itself, forming VGAM1563 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53470] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1563 folded precursor RNA into VGAM1563 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1563 RNA is designated SEQ ID:4274, and is provided hereinbelow with reference to the sequence listing part.

[53471] VGAM1563 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1563 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1563 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53472] VGAM1563 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1563 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1563 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1563 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1563 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53473] The complementary binding of VGAM1563 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1563 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1563 host target RNA into VGAM1563 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53474] It is appreciated that VGAM1563 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1563 host target genes. The mRNA of each one of this plurality of VGAM1563 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1563 RNA, herein designated VGAM RNA, and which when bound by VGAM1563 RNA causes inhibition of translation of respective one or more VGAM1563 host target proteins.

[53475] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1563 gene, herein designated VGAM GENE, on one or more VGAM1563 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[53476] It is yet further appreciated that a function of VGAM1563 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1563 correlate with, and may be deduced from, the identity of the host target genes which VGAM1563 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53477] Nucleotide sequences of the VGAM1563 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1563 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1563 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1563 are further described hereinbelow with reference to Table 1.

[53478] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1563 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1563 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53479] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1563 gene, herein designated VGAM is inhibition of expression of VGAM1563 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1563 correlate with, and may be deduced from, the identity of the target genes which VGAM1563 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53480] Adrenergic, Alpha-1A-, Receptor (ADRA1A, Accession NM\_000680) is a VGAM1563 host target gene. ADRA1A BINDING SITE1 through ADRA1A BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADRA1A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADRA1A BINDING SITE1 through ADRA1A BINDING SITE4, designated SEQ ID:6334, SEQ ID:27135, SEQ ID:27136 and SEQ ID:27134 respectively, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ

ID:4274.

[53481] A function of VGAM1563 is therefore inhibition of Adren-  
ergic, Alpha-1A-, Receptor (ADRA1A, Accession  
NM\_000680). Accordingly, utilities of VGAM1563 include  
diagnosis, prevention and treatment of diseases and clinical  
conditions associated with ADRA1A. Hepatocyte  
Growth Factor (hepapoietin A; scatter factor) (HGF, Acces-  
sion XM\_168542) is another VGAM1563 host target gene.  
HGF BINDING SITE is HOST TARGET binding site found in  
the 3' untranslated region of mRNA encoded by HGF, cor-  
responding to a HOST TARGET binding site such as BIND-  
ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-  
lustrates the complementarity of the nucleotide sequences  
of HGF BINDING SITE, designated SEQ ID:45228, to the  
nucleotide sequence of VGAM1563 RNA, herein desig-  
nated VGAM RNA, also designated SEQ ID:4274.

[53482] Another function of VGAM1563 is therefore inhibition of  
Hepatocyte Growth Factor (hepapoietin A; scatter factor)  
(HGF, Accession XM\_168542), a gene which may be re-  
quired for normal embryonic development; strongly simi-  
lar to murine Hgf, has kringle domains. Accordingly, utili-  
ties of VGAM1563 include diagnosis, prevention and  
treatment of diseases and clinical conditions associated

with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. Occludin (OCLN, Accession NM\_002538) is another VGAM1563 host target gene. OCLN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OCLN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OCLN BINDING SITE, designated SEQ ID:8380, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53483] Another function of VGAM1563 is therefore inhibition of Occludin (OCLN, Accession NM\_002538). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OCLN. Sirtuin Silent Mating Type Information Regulation 2 Homolog 1 (*S. cerevisiae*) (SIRT1, Accession NM\_012238) is another VGAM1563 host target gene. SIRT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIRT1, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIRT1 BINDING SITE, designated SEQ ID:14543, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53484] Another function of VGAM1563 is therefore inhibition of Sirtuin Silent Mating Type Information Regulation 2 Homolog 1 (*S. cerevisiae*) (SIRT1, Accession NM\_012238), a gene which may function as intracellular regulatory protein with mono-ADP-ribosyltransferase activity. Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIRT1. The function of SIRT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM244.CMG2 (Accession NM\_058172) is another VGAM1563 host target gene. CMG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CMG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CMG2 BINDING SITE, designated SEQ

ID:27723, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53485] Another function of VGAM1563 is therefore inhibition of CMG2 (Accession NM\_058172). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CMG2. DKFZp434F142 (Accession NM\_032254) is another VGAM1563 host target gene. DKFZp434F142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434F142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434F142 BINDING SITE, designated SEQ ID:25993, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53486] Another function of VGAM1563 is therefore inhibition of DKFZp434F142 (Accession NM\_032254). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434F142. DKFZp547J036 (Accession

NM\_032281) is another VGAM1563 host target gene. DKFZp547J036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547J036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547J036 BINDING SITE, designated SEQ ID:26041, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53487] Another function of VGAM1563 is therefore inhibition of DKFZp547J036 (Accession NM\_032281). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547J036. Glutamate Receptor, Ionotropic, N-methyl-D-aspartate 3A (GRIN3A, Accession NM\_133445) is another VGAM1563 host target gene. GRIN3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRIN3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN3A BINDING SITE, designated SEQ ID:28539, to the

nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53488] Another function of VGAM1563 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl-D-aspartate 3A (GRIN3A, Accession NM\_133445). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIN3A. KIAA0367 (Accession XM\_041018) is another VGAM1563 host target gene. KIAA0367 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0367, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0367 BINDING SITE, designated SEQ ID:33425, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53489] Another function of VGAM1563 is therefore inhibition of KIAA0367 (Accession XM\_041018). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0367. KIAA0537 (Accession NM\_014840) is another VGAM1563 host target gene. KIAA0537 BINDING SITE is



HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0537, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0537 BINDING SITE, designated SEQ ID:16866, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53490] Another function of VGAM1563 is therefore inhibition of KIAA0537 (Accession NM\_014840). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0537. KIAA1713 (Accession XM\_051335) is another VGAM1563 host target gene. KIAA1713 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1713 BINDING SITE, designated SEQ ID:35811, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53491] Another function of VGAM1563 is therefore inhibition of

KIAA1713 (Accession XM\_051335). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1713. MGC10818 (Accession NM\_030568) is another VGAM1563 host target gene. MGC10818 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10818, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10818 BINDING SITE, designated SEQ ID:24944, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53492] Another function of VGAM1563 is therefore inhibition of MGC10818 (Accession NM\_030568). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10818. PDP (Accession NM\_018444) is another VGAM1563 host target gene. PDP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PDP BINDING SITE, designated SEQ ID:20515, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53493] Another function of VGAM1563 is therefore inhibition of PDP (Accession NM\_018444). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDP. Zinc Finger Protein 323 (ZNF323, Accession NM\_030899) is another VGAM1563 host target gene. ZNF323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF323 BINDING SITE, designated SEQ ID:25171, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53494] Another function of VGAM1563 is therefore inhibition of Zinc Finger Protein 323 (ZNF323, Accession NM\_030899). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF323. LOC146485 (Accession

XM\_007966) is another VGAM1563 host target gene.

LOC146485 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146485, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146485 BINDING SITE, designated SEQ ID:30070, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53495] Another function of VGAM1563 is therefore inhibition of LOC146485 (Accession XM\_007966). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146485. LOC153785 (Accession XM\_087763) is another VGAM1563 host target gene. LOC153785 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153785, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153785 BINDING SITE, designated SEQ ID:39409, to the nucleotide sequence of VGAM1563 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4274.

[53496] Another function of VGAM1563 is therefore inhibition of LOC153785 (Accession XM\_087763). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153785. LOC157663 (Accession XM\_088354) is another VGAM1563 host target gene. LOC157663 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157663 BINDING SITE, designated SEQ ID:39639, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53497] Another function of VGAM1563 is therefore inhibition of LOC157663 (Accession XM\_088354). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157663. LOC158377 (Accession XM\_098933) is another VGAM1563 host target gene. LOC158377 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158377, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158377 BINDING SITE, designated SEQ ID:41970, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53498] Another function of VGAM1563 is therefore inhibition of LOC158377 (Accession XM\_098933). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158377. LOC169611 (Accession XM\_095809) is another VGAM1563 host target gene. LOC169611 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169611, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169611 BINDING SITE, designated SEQ ID:40288, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53499] Another function of VGAM1563 is therefore inhibition of LOC169611 (Accession XM\_095809). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC169611. LOC93624 (Accession XM\_052624) is another VGAM1563 host target gene. LOC93624 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93624 BINDING SITE, designated SEQ ID:36017, to the nucleotide sequence of VGAM1563 RNA, herein designated VGAM RNA, also designated SEQ ID:4274.

[53500] Another function of VGAM1563 is therefore inhibition of LOC93624 (Accession XM\_052624). Accordingly, utilities of VGAM1563 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93624. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1564 (VGAM1564) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53501] VGAM1564 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1564 was detected is described hereinabove with reference to Figs. 1–8.

[53502] VGAM1564 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM1564 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53503] VGAM1564 gene encodes a VGAM1564 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1564 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1564 precursor RNA is designated SEQ ID:1550, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1550 is located at position 167115 relative to the genome of Human Herpesvirus 5.

[53504] VGAM1564 precursor RNA folds onto itself, forming VGAM1564 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by



miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53505] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1564 folded precursor RNA into VGAM1564 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 90%) nucleotide sequence of VGAM1564 RNA is designated SEQ ID:4275, and is provided hereinbelow with reference to the sequence listing part.

[53506] VGAM1564 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1564 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1564 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53507] VGAM1564 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1564 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1564 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1564 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1564 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53508] The complementary binding of VGAM1564 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1564 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1564 host target RNA into VGAM1564 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53509] It is appreciated that VGAM1564 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1564 host target genes. The mRNA of each one of this plurality of VGAM1564 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1564 RNA, herein designated VGAM RNA, and which when bound by VGAM1564 RNA causes inhibition of translation of respective one or more VGAM1564 host target proteins.

[53510] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1564 gene, herein designated VGAM GENE, on one or more VGAM1564 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53511] It is yet further appreciated that a function of VGAM1564 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1564 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1564 correlate with, and may be deduced from, the identity of the host target genes which VGAM1564 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53512] Nucleotide sequences of the VGAM1564 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1564 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1564 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1564 are further described hereinbelow with reference to Table 1.

[53513] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1564 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1564 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53514] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1564 gene, herein designated VGAM is inhibition of expression of VGAM1564 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1564 correlate with, and may be deduced from, the identity of the target genes which VGAM1564 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53515] BMF (Accession NM\_033503) is a VGAM1564 host target gene. BMF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

BMF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMF BINDING SITE, designated SEQ ID:27282, to the nucleotide sequence of VGAM1564 RNA, herein designated VGAM RNA, also designated SEQ ID:4275.

[53516] A function of VGAM1564 is therefore inhibition of BMF (Accession NM\_033503). Accordingly, utilities of VGAM1564 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMF. Chromosome 4 Open Reading Frame 6 (C4orf6, Accession NM\_005750) is another VGAM1564 host target gene. C4orf6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C4orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C4orf6 BINDING SITE, designated SEQ ID:12312, to the nucleotide sequence of VGAM1564 RNA, herein designated VGAM RNA, also designated SEQ ID:4275.

[53517] Another function of VGAM1564 is therefore inhibition of Chromosome 4 Open Reading Frame 6 (C4orf6, Accession

NM\_005750). Accordingly, utilities of VGAM1564 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C4orf6. DKFZp434F142 (Accession NM\_032254) is another VGAM1564 host target gene. DKFZp434F142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434F142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434F142 BINDING SITE, designated SEQ ID:25995, to the nucleotide sequence of VGAM1564 RNA, herein designated VGAM RNA, also designated SEQ ID:4275.

[53518] Another function of VGAM1564 is therefore inhibition of DKFZp434F142 (Accession NM\_032254). Accordingly, utilities of VGAM1564 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434F142. GRB2-associated Binding Protein 3 (GAB3, Accession NM\_080612) is another VGAM1564 host target gene. GAB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of GAB3 BINDING SITE, designated SEQ ID:27930, to the nucleotide sequence of VGAM1564 RNA, herein designated VGAM RNA, also designated SEQ ID:4275.

[53519] Another function of VGAM1564 is therefore inhibition of GRB2-associated Binding Protein 3 (GAB3, Accession NM\_080612). Accordingly, utilities of VGAM1564 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAB3. KIAA0895 (Accession XM\_166573) is another VGAM1564 host target gene. KIAA0895 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0895 BINDING SITE, designated SEQ ID:44548, to the nucleotide sequence of VGAM1564 RNA, herein designated VGAM RNA, also designated SEQ ID:4275.

[53520] Another function of VGAM1564 is therefore inhibition of KIAA0895 (Accession XM\_166573). Accordingly, utilities of VGAM1564 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with KIAA0895. KIAA1193 (Accession XM\_041843) is another VGAM1564 host target gene. KIAA1193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1193 BINDING SITE, designated SEQ ID:33578, to the nucleotide sequence of VGAM1564 RNA, herein designated VGAM RNA, also designated SEQ ID:4275.

[53521] Another function of VGAM1564 is therefore inhibition of KIAA1193 (Accession XM\_041843). Accordingly, utilities of VGAM1564 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1193. MGC2560 (Accession NM\_031452) is another VGAM1564 host target gene. MGC2560 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2560, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2560 BINDING SITE, designated SEQ ID:25468, to the nucleotide

sequence of VGAM1564 RNA, herein designated VGAM RNA, also designated SEQ ID:4275.

[53522] Another function of VGAM1564 is therefore inhibition of MGC2560 (Accession NM\_031452). Accordingly, utilities of VGAM1564 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2560. LOC145497 (Accession XM\_085150) is another VGAM1564 host target gene. LOC145497 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145497 BINDING SITE, designated SEQ ID:37875, to the nucleotide sequence of VGAM1564 RNA, herein designated VGAM RNA, also designated SEQ ID:4275.

[53523] Another function of VGAM1564 is therefore inhibition of LOC145497 (Accession XM\_085150). Accordingly, utilities of VGAM1564 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145497. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1565 (VGAM1565) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53524] VGAM1565 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1565 was detected is described hereinabove with reference to Figs. 1–8.

[53525] VGAM1565 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM1565 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53526] VGAM1565 gene encodes a VGAM1565 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1565 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1565 precursor RNA is designated SEQ ID:1551, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1551 is located at position 170917 relative to the genome of Human Herpesvirus 5.

[53527] VGAM1565 precursor RNA folds onto itself, forming VGAM1565 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53528] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1565 folded precursor RNA into VGAM1565 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1565 RNA is designated SEQ ID:4276, and is provided hereinbelow with reference to the sequence listing part.

[53529] VGAM1565 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1565 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1565 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53530] VGAM1565 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1565 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1565 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1565 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1565 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53531] The complementary binding of VGAM1565 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1565 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1565 host target RNA into VGAM1565 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53532] It is appreciated that VGAM1565 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1565 host target genes. The mRNA of each one of this plurality of VGAM1565 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1565 RNA, herein designated VGAM RNA, and which when bound by VGAM1565 RNA causes inhibition of translation of respective one or more VGAM1565 host target proteins.

[53533] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1565 gene, herein designated VGAM GENE, on one or more VGAM1565 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53534] It is yet further appreciated that a function of VGAM1565 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1565 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1565 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53535] Nucleotide sequences of the VGAM1565 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1565 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1565 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1565 are further described hereinbelow with reference to Table 1.

[53536] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1565 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1565 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53537] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1565 gene, herein designated VGAM is inhibition of expression of VGAM1565 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1565 correlate with, and may be deduced from, the identity of the target genes which VGAM1565



binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53538] ATP-binding Cassette, Sub-family F (GCN20), Member 1 (ABCF1, Accession NM\_001090) is a VGAM1565 host target gene. ABCF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCF1 BINDING SITE, designated SEQ ID:6746, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53539] A function of VGAM1565 is therefore inhibition of ATP-binding Cassette, Sub-family F (GCN20), Member 1 (ABCF1, Accession NM\_001090). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCF1. Carbohydrate Kinase-like (CARKL, Accession NM\_013276) is another VGAM1565 host target gene. CARKL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARKL, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARKL BINDING SITE, designated SEQ ID:14938, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53540] Another function of VGAM1565 is therefore inhibition of Carbohydrate Kinase-like (CARKL, Accession NM\_013276), a gene which is a putative carbohydrate kinase and may be a modifier for the cystinosis phenotype. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARKL. The function of CARKL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM419. Cryptochrome 2 (photolyase-like) (CRY2, Accession XM\_051030) is another VGAM1565 host target gene. CRY2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRY2 BINDING SITE, designated SEQ ID:35731, to the nucleotide sequence of

VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53541] Another function of VGAM1565 is therefore inhibition of Cryptochrome 2 (photolyase-like) (CRY2, Accession XM\_051030), a gene which has a role in circadian photoreception in mammals. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRY2. The function of CRY2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1223. Diacylglycerol O-acyltransferase Homolog 2 (mouse) (DGAT2, Accession NM\_032564) is another VGAM1565 host target gene. DGAT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DGAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGAT2 BINDING SITE, designated SEQ ID:26292, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53542] Another function of VGAM1565 is therefore inhibition of

Diacylglycerol O-acyltransferase Homolog 2 (mouse) (DGAT2, Accession NM\_032564). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGAT2. Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM\_004021) is another VGAM1565 host target gene. DMD BINDING SITE1 through DMD BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DMD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMD BINDING SITE1 through DMD BINDING SITE3, designated SEQ ID:10222, SEQ ID:10234 and SEQ ID:10195 respectively, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53543] Another function of VGAM1565 is therefore inhibition of Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM\_004021), a gene which muscular dystrophy . Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMD. The function of

DMD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM218.UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 3 (GalNAc-T3) (GALNT3, Accession NM\_004482) is another VGAM1565 host target gene. GALNT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALNT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT3 BINDING SITE, designated SEQ ID:10802, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53544] Another function of VGAM1565 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 3 (GalNAc-T3) (GALNT3, Accession NM\_004482), a gene which initiates O-glycosylation of serine and threonine residues. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT3. The function of GALNT3 has been es-

established by previous studies. GALNT3 (EC 2.4.1.41) is one of several enzymes that catalyze the reaction  $\text{UDP-GalNAc} + \text{polypeptide-(Ser/Thr)-OH} \rightarrow \text{GalNAc-}\alpha\text{-O-Ser/Thr-polypeptide} + \text{UDP}$ , thereby initiating O-glycosylation of serine and threonine residues on an array of glycoproteins. Bennett et al. (1996) used degenerate PCR to clone human GALNT3 using primers based on the sequences of GALNT1 (OMIM Ref. No. 602273) and GALNT2 (OMIM Ref. No. 602274). GALNT3 encodes a 633-amino acid protein which has a single membrane-spanning region and is highly homologous to GALNT1 and GALNT2. Northern blot analysis showed that GALNT3 is expressed as a 3.6-kb transcript, with highest levels in human pancreas and testis. Bennett et al. (1996) expressed the gene in insect Sf9 cells and showed that GALNT3 does have GalNAc-transferase activity, but with different substrate specificity than GALNT1 or GALNT2. The mouse ortholog of GalNAc-T3 was cloned by Zara et al. (1996). Bennett et al. (1998) found that the GALNT1, GALNT2, and GALNT3 genes contain 11, 16, and 10 exons, respectively. Several intron/exon boundaries are conserved within the 3 genes. By FISH, Bennett et al. (1998) mapped the GALNT3 gene to human chromosome

2q24-q31.

[53545] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53546] Bennett, E. P.; Hassan, H.; Clausen, H. : cDNA cloning and expression of a novel human UDP-N-acetyl-alpha-D-galactosamine. J. Biol. Chem. 271: 17006-17012, 1996. ; and

[53547] Bennett, E. P.; Weghuis, D. O.; Merkx, G.; Geurts van Kessel, A.; Eiberg, H.; Clausen, H. : Genomic organization and chromosomal localization of three members of the UDP-N-acetylgalacto.

[53548] Further studies establishing the function and utilities of GALNT3 are found in John Hopkins OMIM database record ID 601756, and in cited publications numbered 2823-2825 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Host Cell Factor C1 (VP16-accessory protein) (HCFC1, Accession XM\_048390) is another VGAM1565 host target gene. HCFC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCFC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of HCFC1 BINDING SITE, designated SEQ ID:35158, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53549] Another function of VGAM1565 is therefore inhibition of Host Cell Factor C1 (VP16-accessory protein) (HCFC1, Accession XM\_048390), a gene which is a host cell factor, has a role in cell proliferation and can form a complex with HSV VP16. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCFC1. The function of HCFC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM341.Homeo Box A7 (HOXA7, Accession NM\_006896) is another VGAM1565 host target gene. HOXA7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HOXA7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXA7 BINDING SITE, designated SEQ ID:13769, to the



nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53550] Another function of VGAM1565 is therefore inhibition of Homeo Box A7 (HOXA7, Accession NM\_006896), a gene which provides cells with specific positional identities on the anterior–posterior axis. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXA7. The function of HOXA7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Potassium Voltage–gated Channel, Shaker–related Subfamily, Beta Member 1 (KCNAB1, Accession XM\_027634) is another VGAM1565 host target gene. KCNAB1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KCNAB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNAB1 BINDING SITE, designated SEQ ID:30546, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53551] Another function of VGAM1565 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Beta Member 1 (KCNAB1, Accession XM\_027634), a gene which is the regulatory beta subunit for a shaker-related voltage-gated potassium channel. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNAB1. The function of KCNAB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM727. Lamin B Receptor (LBR, Accession XM\_001795) is another VGAM1565 host target gene. LBR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LBR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LBR BINDING SITE, designated SEQ ID:29852, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53552] Another function of VGAM1565 is therefore inhibition of Lamin B Receptor (LBR, Accession XM\_001795). Accordingly, utilities of VGAM1565 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with LBR. LIM Domain Only 7 (LMO7, Accession NM\_015843) is another VGAM1565 host target gene. LMO7 BINDING SITE1 and LMO7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LMO7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMO7 BINDING SITE1 and LMO7 BINDING SITE2, designated SEQ ID:17970 and SEQ ID:11827 respectively, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53553] Another function of VGAM1565 is therefore inhibition of LIM Domain Only 7 (LMO7, Accession NM\_015843). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMO7. Ribonuclease, RNase A Family, 1 (pancreatic) (RNASE1, Accession XM\_033595) is another VGAM1565 host target gene. RNASE1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RNASE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNASE1 BINDING SITE, designated SEQ ID:31945, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53554] Another function of VGAM1565 is therefore inhibition of Ribonuclease, RNase A Family, 1 (pancreatic) (RNASE1, Accession XM\_033595), a gene which is a Pancreatic ribonuclease; a pyrimidine-specific endonuclease that generates 2',3'-cyclic phosphate products. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNASE1. The function of RNASE1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM210.RNA (guanine-7-) Methyltransferase (RNMT, Accession NM\_003799) is another VGAM1565 host target gene. RNMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNMT BINDING SITE,

designated SEQ ID:9889, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53555] Another function of VGAM1565 is therefore inhibition of RNA (guanine-7-) Methyltransferase (RNMT, Accession NM\_003799), a gene which catalyzes the methylation of GpppN- at the guanine N7 position. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNMT. The function of RNMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754) is another VGAM1565 host target gene. RUNX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RUNX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RUNX1 BINDING SITE, designated SEQ ID:7500, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ

ID:4276.

[53556] Another function of VGAM1565 is therefore inhibition of Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RUNX1. Synuclein, Alpha (non A4 component of amyloid precursor) (SNCA, Accession NM\_000345) is another VGAM1565 host target gene. SNCA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNCA BINDING SITE, designated SEQ ID:5896, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53557] Another function of VGAM1565 is therefore inhibition of Synuclein, Alpha (non A4 component of amyloid precursor) (SNCA, Accession NM\_000345). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNCA. Ubiquitin Specific Protease 6 (Tre-2 oncogene)

(USP6, Accession XM\_165948) is another VGAM1565 host target gene. USP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP6 BINDING SITE, designated SEQ ID:43810, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53558] Another function of VGAM1565 is therefore inhibition of Ubiquitin Specific Protease 6 (Tre-2 oncogene) (USP6, Accession XM\_165948), a gene which has an atp-independent isopeptidase activity, cleaving at the carboxyl terminus of the ubiquitin moiety. Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP6. The function of USP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM296. Amyotrophic Lateral Sclerosis 2 (juvenile) Chromosome Region, Candidate 3 (ALS2CR3, Accession NM\_015049) is another VGAM1565 host target gene.

ALS2CR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALS2CR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALS2CR3 BINDING SITE, designated SEQ ID:17412, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53559] Another function of VGAM1565 is therefore inhibition of Amyotrophic Lateral Sclerosis 2 (juvenile) Chromosome Region, Candidate 3 (ALS2CR3, Accession NM\_015049). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALS2CR3. CD36L2 (Accession NM\_005506) is another VGAM1565 host target gene. CD36L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD36L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD36L2 BINDING SITE, designated SEQ ID:12020, to the nucleotide sequence of VGAM1565 RNA,



herein designated VGAM RNA, also designated SEQ ID:4276.

[53560] Another function of VGAM1565 is therefore inhibition of CD36L2 (Accession NM\_005506). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD36L2. Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM\_004734) is another VGAM1565 host target gene. DCAMKL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCAMKL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCAMKL1 BINDING SITE, designated SEQ ID:11117, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53561] Another function of VGAM1565 is therefore inhibition of Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM\_004734). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCAMKL1. FKSG28 (Accession NM\_030929) is another VGAM1565 host target

gene. FKSG28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FKSG28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKSG28 BINDING SITE, designated SEQ ID:25202, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53562] Another function of VGAM1565 is therefore inhibition of FKSG28 (Accession NM\_030929). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKSG28. KIAA0173 (Accession NM\_014640) is another VGAM1565 host target gene. KIAA0173 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0173 BINDING SITE, designated SEQ ID:16041, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53563] Another function of VGAM1565 is therefore inhibition of KIAA0173 (Accession NM\_014640). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0173. KIAA0317 (Accession NM\_014821) is another VGAM1565 host target gene. KIAA0317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0317 BINDING SITE, designated SEQ ID:16793, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53564] Another function of VGAM1565 is therefore inhibition of KIAA0317 (Accession NM\_014821). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0317. KIAA0663 (Accession NM\_014827) is another VGAM1565 host target gene. KIAA0663 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0663, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0663 BINDING SITE, designated SEQ ID:16813, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53565] Another function of VGAM1565 is therefore inhibition of KIAA0663 (Accession NM\_014827). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0663. KIAA1001 (Accession NM\_014960) is another VGAM1565 host target gene. KIAA1001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1001 BINDING SITE, designated SEQ ID:17328, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53566] Another function of VGAM1565 is therefore inhibition of KIAA1001 (Accession NM\_014960). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1001. KIAA1128 (Accession XM\_043596) is another VGAM1565 host target gene. KIAA1128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1128 BINDING SITE, designated SEQ ID:33971, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53567] Another function of VGAM1565 is therefore inhibition of KIAA1128 (Accession XM\_043596). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1128. Karyopherin Alpha 6 (importin alpha 7) (KPNA6, Accession NM\_012316) is another VGAM1565 host target gene. KPNA6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KPNA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KPNA6 BINDING SITE, designated SEQ ID:14685, to the nucleotide sequence of

VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53568] Another function of VGAM1565 is therefore inhibition of Karyopherin Alpha 6 (importin alpha 7) (KPNA6, Accession NM\_012316). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KPNA6. Nucleoporin 54kDa (NUP54, Accession XM\_011144) is another VGAM1565 host target gene. NUP54 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUP54, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUP54 BINDING SITE, designated SEQ ID:30179, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53569] Another function of VGAM1565 is therefore inhibition of Nucleoporin 54kDa (NUP54, Accession XM\_011144). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUP54. Tumor Necrosis Factor Receptor Superfamily, Member 21 (TNFRSF21, Accession

NM\_014452) is another VGAM1565 host target gene. TNFRSF21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF21 BINDING SITE, designated SEQ ID:15803, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53570] Another function of VGAM1565 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 21 (TNFRSF21, Accession NM\_014452). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF21. LOC158527 (Accession XM\_088594) is another VGAM1565 host target gene. LOC158527 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158527 BINDING SITE, designated SEQ ID:39861, to

the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53571] Another function of VGAM1565 is therefore inhibition of LOC158527 (Accession XM\_088594). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158527. LOC162239 (Accession XM\_091439) is another VGAM1565 host target gene. LOC162239 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC162239, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162239 BINDING SITE, designated SEQ ID:40052, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53572] Another function of VGAM1565 is therefore inhibition of LOC162239 (Accession XM\_091439). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162239. LOC220477 (Accession XM\_071675) is another VGAM1565 host target gene. LOC220477 BINDING SITE is HOST TARGET binding site found in the 5' un-



translated region of mRNA encoded by LOC220477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220477 BINDING SITE, designated SEQ ID:37409, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53573] Another function of VGAM1565 is therefore inhibition of LOC220477 (Accession XM\_071675). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220477. LOC220573 (Accession XM\_045569) is another VGAM1565 host target gene. LOC220573 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220573 BINDING SITE, designated SEQ ID:34484, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53574] Another function of VGAM1565 is therefore inhibition of LOC220573 (Accession XM\_045569). Accordingly, utilities

of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220573. LOC221337 (Accession XM\_166387) is another VGAM1565 host target gene. LOC221337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221337 BINDING SITE, designated SEQ ID:44236, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53575] Another function of VGAM1565 is therefore inhibition of LOC221337 (Accession XM\_166387). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221337. LOC253019 (Accession XM\_170907) is another VGAM1565 host target gene. LOC253019 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC253019 BINDING SITE, designated SEQ ID:45668, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53576] Another function of VGAM1565 is therefore inhibition of LOC253019 (Accession XM\_170907). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253019. LOC253975 (Accession XM\_171130) is another VGAM1565 host target gene. LOC253975 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253975, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253975 BINDING SITE, designated SEQ ID:45935, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53577] Another function of VGAM1565 is therefore inhibition of LOC253975 (Accession XM\_171130). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253975. LOC51279 (Accession NM\_016546) is another VGAM1565 host target gene. LOC51279 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51279, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51279 BINDING SITE, designated SEQ ID:18615, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53578] Another function of VGAM1565 is therefore inhibition of LOC51279 (Accession NM\_016546). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51279. LOC93190 (Accession XM\_049705) is another VGAM1565 host target gene. LOC93190 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC93190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93190 BINDING SITE, designated SEQ ID:35489, to the nucleotide sequence of VGAM1565 RNA, herein designated VGAM RNA, also designated SEQ ID:4276.

[53579] Another function of VGAM1565 is therefore inhibition of

LOC93190 (Accession XM\_049705). Accordingly, utilities of VGAM1565 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93190. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1566 (VGAM1566) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53580] VGAM1566 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1566 was detected is described hereinabove with reference to Figs. 1-8.

[53581] VGAM1566 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM1566 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53582] VGAM1566 gene encodes a VGAM1566 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1566 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1566 precursor RNA is designated SEQ ID:1552, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1552 is located at position 165653 relative to the genome of Human Herpesvirus 5.

- [53583] VGAM1566 precursor RNA folds onto itself, forming VGAM1566 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [53584] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1566 folded precursor RNA into VGAM1566 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide se-

quence of VGAM1566 RNA is designated SEQ ID:4277, and is provided hereinbelow with reference to the sequence listing part.

[53585] VGAM1566 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1566 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1566 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53586] VGAM1566 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1566 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1566 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1566 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1566 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[53587] The complementary binding of VGAM1566 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1566 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1566 host target RNA into VGAM1566 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53588] It is appreciated that VGAM1566 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1566 host target genes. The mRNA of each one of this plurality of VGAM1566 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1566 RNA, herein designated VGAM RNA, and which when bound by VGAM1566 RNA causes inhibition of translation of respective one or more VGAM1566 host target proteins.

[53589] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1566 gene, herein designated VGAM GENE, on one or more VGAM1566 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53590] It is yet further appreciated that a function of VGAM1566

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1566 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1566 correlate with, and may be deduced from, the identity of the host target genes which VGAM1566 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53591] Nucleotide sequences of the VGAM1566 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1566 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1566 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1566 are further described hereinbelow with reference to Table 1.

[53592] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1566 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1566 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53593] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1566 gene, herein designated VGAM is inhibition of expression of VGAM1566 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1566 correlate with, and may be deduced from, the identity of the target genes which VGAM1566 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53594] Ankylosis, Progressive Homolog (mouse) (ANKH, Accession NM\_054027) is a VGAM1566 host target gene. ANKH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKH BINDING SITE, designated SEQ ID:27636, to the nucleotide sequence of VGAM1566 RNA, herein designated VGAM RNA, also designated SEQ ID:4277.

[53595] A function of VGAM1566 is therefore inhibition of Ankylosis, Progressive Homolog (mouse) (ANKH, Accession NM\_054027), a gene which regulates intra- and extracellular levels of inorganic pyrophosphate (ppi), probably functioning as ppi transporter. Accordingly, utilities of

VGAM1566 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKH. The function of ANKH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1247. Sialic Acid Binding Ig-like Lectin 6 (SIGLEC6, Accession XM\_009378) is another VGAM1566 host target gene. SIGLEC6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIGLEC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIGLEC6 BINDING SITE, designated SEQ ID:30109, to the nucleotide sequence of VGAM1566 RNA, herein designated VGAM RNA, also designated SEQ ID:4277.

[53596] Another function of VGAM1566 is therefore inhibition of Sialic Acid Binding Ig-like Lectin 6 (SIGLEC6, Accession XM\_009378), a gene which is a cell adhesion molecule for postnatal neural development. Accordingly, utilities of VGAM1566 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIGLEC6. The function of SIGLEC6 has been established by

previous studies. Molecules belonging to the immunoglobulin (Ig) superfamily function as mediators of cell-cell interactions. The sialoadhesin family, a group of sialic acid-binding proteins, is a subgroup of the Ig superfamily. Members of the sialoadhesin family include myeloid antigen CD33 (OMIM Ref. No. 159590). By sequencing cDNAs randomly selected from a human placenta cDNA library, Takei et al. (1997) identified a partial cDNA with high sequence similarity to CD33. Using the partial cDNA, they isolated full-length placenta cDNAs. Since the predicted protein had significant similarity to CD33, they called the corresponding gene 'CD33 antigen-like' (CD33L). The deduced 442-amino acid CD33L protein contains a signal peptide, an N-terminal Ig-like V-domain, and 2 adjacent Ig C2-like domains, followed by a transmembrane region and a cytoplasmic tail. Based on its predicted structure, the authors stated that CD33L belongs to the Ig superfamily and is likely a novel member of the sialoadhesin subfamily. Takei et al. (1997) also isolated a cDNA likely representing an alternatively spliced CD33L transcript; they called this transcript CD33L2 and the aforementioned transcript CD33L1. Compared to the original cDNA, this cDNA contains a 176-bp deletion in

the coding sequence, resulting in a predicted 342–amino acid protein lacking the transmembrane and cytoplasmic regions. By RT–PCR of placenta RNA, the authors detected both transcripts, although the transcript encoding the membrane–bound isoform, CD33L1, was considerably more abundant. Northern blot analysis of 16 adult tissues and 4 fetal tissues detected CD33L expression only in the placenta; transcripts of 4 distinct sizes were found, including 1 that was differentially polyadenylated. Using an expression cloning strategy to identify molecules that bind to leptin (OMIM Ref. No. 164160), Patel et al. (1999) isolated a human erythroleukemic cell line cDNA encoding OBBP1. They stated that OBBP1 is identical to CD33L (Takei et al., 1997). The deduced 441–amino acid OBBP1 protein shares 63% and 59% sequence identity with CD33 and OBBP2 (SIGLEC5; 604200), respectively. All 3 of these proteins have a cytoplasmic domain containing putative sites of tyrosine phosphorylation, including an immunoreceptor tyrosine kinase inhibitory motif and a motif found in SLAM (OMIM Ref. No. 603492) and SLAM–like proteins. In vitro studies with sialylated ligands indicated that OBBP1 selectively bound to Neu5Ac(alpha)2–6GalNAc(alpha), or sialyl–Tn, allowing its

formal designation as a SIGLEC (sialic acid-binding Ig-like lectin). Recombinant OBBP1 exhibited tight and specific binding to leptin, whereas OBBP2 and CD33 bound weakly to leptin. Northern blot analysis detected high expression of OBBP1 mRNA in placenta, with moderate expression in peripheral blood leukocytes, spleen, and small intestine. Immunohistochemical analysis showed that OBBP1 is highly expressed in the cyto- and syncytiotrophoblasts of the placenta. Flow cytometric analysis on peripheral blood leukocytes found that OBBP1 is almost exclusively expressed on B cells.

[53597] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53598] Patel, N.; Brinkman-Van der Linden, E. C. M.; Altmann, S. W.; Gish, K.; Balasubramanian, S.; Timans, J. C.; Peterson, D.; Bell, M. P.; Bazan, J. F.; Varki, A.; Kastelein, R. A. : OBBP1/Siglec-6: a leptin- and sialic acid-binding protein of the immunoglobulin superfamily. *J. Biol. Chem.* 274: 22729-22738, 1999. Note: Erratum: *J. Biol. Chem.* 274: 28058 only, 1999. ; and

[53599] Takei, Y.; Sasaki, S.; Fujiwara, T.; Takahashi, E.; Muto, T.; Nakamura, Y. : Molecular cloning of a novel gene similar

to myeloid antigen CD33 and its specific expression in placenta.

[53600] Further studies establishing the function and utilities of SIGLEC6 are found in John Hopkins OMIM database record ID 604405, and in cited publications numbered 707 and 7444 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ14596 (Accession NM\_032809) is another VGAM1566 host target gene. FLJ14596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14596 BINDING SITE, designated SEQ ID:26569, to the nucleotide sequence of VGAM1566 RNA, herein designated VGAM RNA, also designated SEQ ID:4277.

[53601] Another function of VGAM1566 is therefore inhibition of FLJ14596 (Accession NM\_032809). Accordingly, utilities of VGAM1566 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14596. LOC147276 (Accession XM\_085756) is another VGAM1566 host target gene. LOC147276 BINDING SITE is



HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147276 BINDING SITE, designated SEQ ID:38327, to the nucleotide sequence of VGAM1566 RNA, herein designated VGAM RNA, also designated SEQ ID:4277.

[53602] Another function of VGAM1566 is therefore inhibition of LOC147276 (Accession XM\_085756). Accordingly, utilities of VGAM1566 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147276. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1567 (VGAM1567) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53603] VGAM1567 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1567 was detected is described hereinabove with reference to Figs. 1-8.

[53604] VGAM1567 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM1567 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53605] VGAM1567 gene encodes a VGAM1567 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1567 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1567 precursor RNA is designated SEQ ID:1553, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1553 is located at position 69308 relative to the genome of Human Herpesvirus 5.

[53606] VGAM1567 precursor RNA folds onto itself, forming VGAM1567 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[53607] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1567 folded precursor RNA into VGAM1567 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1567 RNA is designated SEQ ID:4278, and is provided hereinbelow with reference to the sequence listing part.

[53608] VGAM1567 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1567 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1567 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53609] VGAM1567 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1567 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1567 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1567 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1567 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53610] The complementary binding of VGAM1567 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1567 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1567 host target RNA into VGAM1567 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53611] It is appreciated that VGAM1567 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1567 host target genes. The mRNA of each one of this plurality of VGAM1567 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1567 RNA, herein designated VGAM RNA, and which when bound by VGAM1567 RNA causes inhibition of translation of respective one or more VGAM1567 host target proteins.

[53612] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1567 gene, herein designated VGAM GENE, on one or more VGAM1567 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53613] It is yet further appreciated that a function of VGAM1567 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1567 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1567 correlate with, and may be deduced from, the identity of the host target genes which VGAM1567 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53614] Nucleotide sequences of the VGAM1567 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1567 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1567 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1567 are further described hereinbelow with reference to Table 1.

[53615] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1567 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1567 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53616] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1567 gene, herein designated VGAM is inhibition of expression of VGAM1567 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1567 correlate with, and may be deduced from, the identity of the target genes which VGAM1567 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53617] Fibroblast Activation Protein, Alpha (FAP, Accession NM\_004460) is a VGAM1567 host target gene. FAP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates

the complementarity of the nucleotide sequences of FAP BINDING SITE, designated SEQ ID:10765, to the nucleotide sequence of VGAM1567 RNA, herein designated VGAM RNA, also designated SEQ ID:4278.

[53618] A function of VGAM1567 is therefore inhibition of Fibroblast Activation Protein, Alpha (FAP, Accession NM\_004460), a gene which may have a role in tissue remodeling during development and wound healing. Accordingly, utilities of VGAM1567 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAP. The function of FAP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM927. LOC145739 (Accession XM\_085222) is another VGAM1567 host target gene. LOC145739 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145739 BINDING SITE, designated SEQ ID:37965, to the nucleotide sequence of VGAM1567 RNA, herein designated VGAM RNA, also des-



ignated SEQ ID:4278.

[53619] Another function of VGAM1567 is therefore inhibition of LOC145739 (Accession XM\_085222). Accordingly, utilities of VGAM1567 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145739. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1568 (VGAM1568) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53620] VGAM1568 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1568 was detected is described hereinabove with reference to Figs. 1–8.

[53621] VGAM1568 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM1568 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53622] VGAM1568 gene encodes a VGAM1568 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1568 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1568 precursor RNA is designated SEQ ID:1554, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1554 is located at position 61146 relative to the genome of Human Herpesvirus 5.

- [53623] VGAM1568 precursor RNA folds onto itself, forming VGAM1568 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [53624] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1568 folded precursor RNA into VGAM1568 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1568 RNA is designated SEQ ID:4279, and is provided hereinbelow with reference to the sequence listing part.

[53625] VGAM1568 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1568 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1568 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53626] VGAM1568 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1568 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1568 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1568 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1568 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[53627] The complementary binding of VGAM1568 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1568 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1568 host target RNA into VGAM1568 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53628] It is appreciated that VGAM1568 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1568 host target genes. The mRNA of

each one of this plurality of VGAM1568 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1568 RNA, herein designated VGAM RNA, and which when bound by VGAM1568 RNA causes inhibition of translation of respective one or more VGAM1568 host target proteins.

[53629] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1568 gene, herein designated VGAM GENE, on one or more VGAM1568 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[53630] It is yet further appreciated that a function of VGAM1568 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1568 correlate with, and may be deduced from, the identity of the host target genes which VGAM1568 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53631] Nucleotide sequences of the VGAM1568 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1568 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1568 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1568 are further described hereinbelow with reference to Table 1.

[53632] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1568 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1568 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53633] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1568 gene, herein designated VGAM is inhibition of expression of VGAM1568 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1568 correlate with, and may be deduced from, the identity of the target genes which VGAM1568 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53634] Protein Kinase C and Casein Kinase Substrate In Neurons 1 (PACSIN1, Accession XM\_166424) is a VGAM1568 host target gene. PACSIN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACSIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACSIN1 BINDING SITE, designated SEQ ID:44317, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53635] A function of VGAM1568 is therefore inhibition of Protein Kinase C and Casein Kinase Substrate In Neurons 1

(PACSIN1, Accession XM\_166424). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACSIN1. FLJ22060 (Accession NM\_024612) is another VGAM1568 host target gene. FLJ22060 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22060 BINDING SITE, designated SEQ ID:23864, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53636] Another function of VGAM1568 is therefore inhibition of FLJ22060 (Accession NM\_024612). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22060. GLP (Accession NM\_018652) is another VGAM1568 host target gene. GLP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity



of the nucleotide sequences of GLP BINDING SITE, designated SEQ ID:20724, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53637] Another function of VGAM1568 is therefore inhibition of GLP (Accession NM\_018652). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLP. GOLGIN-67 (Accession XM\_170772) is another VGAM1568 host target gene. GOLGIN-67 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLGIN-67, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGIN-67 BINDING SITE, designated SEQ ID:45537, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53638] Another function of VGAM1568 is therefore inhibition of GOLGIN-67 (Accession XM\_170772). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGIN-67. KIAA0855 (Accession NM\_015003) is another

VGAM1568 host target gene. KIAA0855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0855 BINDING SITE, designated SEQ ID:17377, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53639] Another function of VGAM1568 is therefore inhibition of KIAA0855 (Accession NM\_015003). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0855. Zinc Finger Protein 238 (ZNF238, Accession NM\_006352) is another VGAM1568 host target gene. ZNF238 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF238, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF238 BINDING SITE, designated SEQ ID:13046, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ

ID:4279.

[53640] Another function of VGAM1568 is therefore inhibition of Zinc Finger Protein 238 (ZNF238, Accession NM\_006352). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF238. LOC204301 (Accession XM\_115306) is another VGAM1568 host target gene. LOC204301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204301 BINDING SITE, designated SEQ ID:43095, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53641] Another function of VGAM1568 is therefore inhibition of LOC204301 (Accession XM\_115306). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204301. LOC220534 (Accession XM\_165405) is another VGAM1568 host target gene. LOC220534 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC220534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220534 BINDING SITE, designated SEQ ID:43618, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53642] Another function of VGAM1568 is therefore inhibition of LOC220534 (Accession XM\_165405). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220534. LOC220538 (Accession XM\_165407) is another VGAM1568 host target gene. LOC220538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220538 BINDING SITE, designated SEQ ID:43628, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53643] Another function of VGAM1568 is therefore inhibition of LOC220538 (Accession XM\_165407). Accordingly, utilities

of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220538. LOC220963 (Accession XM\_166145) is another VGAM1568 host target gene. LOC220963 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220963, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220963 BINDING SITE, designated SEQ ID:43959, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53644] Another function of VGAM1568 is therefore inhibition of LOC220963 (Accession XM\_166145). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220963. LOC254358 (Accession XM\_170771) is another VGAM1568 host target gene. LOC254358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC254358 BINDING SITE, designated SEQ ID:45533, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53645] Another function of VGAM1568 is therefore inhibition of LOC254358 (Accession XM\_170771). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254358. LOC257286 (Accession XM\_170549) is another VGAM1568 host target gene. LOC257286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257286 BINDING SITE, designated SEQ ID:45375, to the nucleotide sequence of VGAM1568 RNA, herein designated VGAM RNA, also designated SEQ ID:4279.

[53646] Another function of VGAM1568 is therefore inhibition of LOC257286 (Accession XM\_170549). Accordingly, utilities of VGAM1568 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257286. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1569 (VGAM1569) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53647] VGAM1569 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1569 was detected is described hereinabove with reference to Figs. 1–8.

[53648] VGAM1569 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM1569 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53649] VGAM1569 gene encodes a VGAM1569 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1569 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1569 precursor RNA is designated SEQ ID:1555, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1555 is located at position 66671 relative to the

genome of Human Herpesvirus 5.

[53650] VGAM1569 precursor RNA folds onto itself, forming VGAM1569 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53651] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1569 folded precursor RNA into VGAM1569 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1569 RNA is designated SEQ ID:4280, and is provided hereinbelow with reference to the sequence listing part.

[53652] VGAM1569 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1569 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1569 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53653] VGAM1569 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1569 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1569 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1569 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1569 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53654] The complementary binding of VGAM1569 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1569 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1569 host target RNA into VGAM1569 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53655] It is appreciated that VGAM1569 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1569 host target genes. The mRNA of each one of this plurality of VGAM1569 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1569 RNA, herein designated VGAM RNA, and which when bound by VGAM1569 RNA causes inhibition of translation of respective one or more VGAM1569 host target proteins.

[53656] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1569 gene, herein designated VGAM GENE, on one or more VGAM1569 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53657] It is yet further appreciated that a function of VGAM1569 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1569 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1569

correlate with, and may be deduced from, the identity of the host target genes which VGAM1569 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53658] Nucleotide sequences of the VGAM1569 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1569 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1569 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1569 are further described hereinbelow with reference to Table 1.

[53659] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1569 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1569 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53660] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1569 gene, herein designated VGAM is inhibition of expression of VGAM1569 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1569 correlate with, and may be deduced

from, the identity of the target genes which VGAM1569 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53661] MAP/microtubule Affinity-regulating Kinase 3 (MARK3, Accession NM\_002376) is a VGAM1569 host target gene. MARK3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MARK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MARK3 BINDING SITE, designated SEQ ID:8189, to the nucleotide sequence of VGAM1569 RNA, herein designated VGAM RNA, also designated SEQ ID:4280.

[53662] A function of VGAM1569 is therefore inhibition of MAP/microtubule Affinity-regulating Kinase 3 (MARK3, Accession NM\_002376), a gene which may be involved in cell cycle regulation. Accordingly, utilities of VGAM1569 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MARK3. The function of MARK3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM964.Testis Expressed Sequence 15 (TEX15, Accession NM\_031271) is another VGAM1569 host target gene. TEX15 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TEX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEX15 BINDING SITE, designated SEQ ID:25295, to the nucleotide sequence of VGAM1569 RNA, herein designated VGAM RNA, also designated SEQ ID:4280.

[53663] Another function of VGAM1569 is therefore inhibition of Testis Expressed Sequence 15 (TEX15, Accession NM\_031271). Accordingly, utilities of VGAM1569 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEX15. Tumor Protein P63 (TP63, Accession NM\_003722) is another VGAM1569 host target gene. TP63 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TP63, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP63 BINDING SITE, designated SEQ ID:9817,

to the nucleotide sequence of VGAM1569 RNA, herein designated VGAM RNA, also designated SEQ ID:4280.

[53664] Another function of VGAM1569 is therefore inhibition of Tumor Protein P63 (TP63, Accession NM\_003722). Accordingly, utilities of VGAM1569 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP63. G-protein Coupled Receptor 88 (GPR88, Accession NM\_022049) is another VGAM1569 host target gene. GPR88 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR88, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR88 BINDING SITE, designated SEQ ID:22572, to the nucleotide sequence of VGAM1569 RNA, herein designated VGAM RNA, also designated SEQ ID:4280.

[53665] Another function of VGAM1569 is therefore inhibition of G-protein Coupled Receptor 88 (GPR88, Accession NM\_022049). Accordingly, utilities of VGAM1569 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR88. LOC223009 (Accession XM\_170214) is another VGAM1569 host target

gene. LOC223009 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC223009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC223009 BINDING SITE, designated SEQ ID:45314, to the nucleotide sequence of VGAM1569 RNA, herein designated VGAM RNA, also designated SEQ ID:4280.

[53666] Another function of VGAM1569 is therefore inhibition of LOC223009 (Accession XM\_170214). Accordingly, utilities of VGAM1569 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC223009. LOC254173 (Accession XM\_173022) is another VGAM1569 host target gene. LOC254173 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC254173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254173 BINDING SITE, designated SEQ ID:46288, to the nucleotide sequence of VGAM1569 RNA, herein designated VGAM RNA, also designated SEQ ID:4280.



[53667] Another function of VGAM1569 is therefore inhibition of LOC254173 (Accession XM\_173022). Accordingly, utilities of VGAM1569 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254173. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1570 (VGAM1570) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53668] VGAM1570 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1570 was detected is described hereinabove with reference to Figs. 1–8.

[53669] VGAM1570 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM1570 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53670] VGAM1570 gene encodes a VGAM1570 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1570 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1570 precursor RNA is designated SEQ ID:1556, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1556 is located at position 65530 relative to the genome of Human Herpesvirus 5.

[53671] VGAM1570 precursor RNA folds onto itself, forming VGAM1570 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53672] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1570 folded precursor RNA into VGAM1570 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1570 RNA is designated SEQ ID:4281, and is provided hereinbelow with reference to the sequence listing part.

[53673] VGAM1570 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1570 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1570 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[53674] VGAM1570 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1570 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1570 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1570 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1570 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53675] The complementary binding of VGAM1570 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1570 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1570 host target RNA into VGAM1570 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53676] It is appreciated that VGAM1570 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1570 host target genes. The mRNA of each one of this plurality of VGAM1570 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1570 RNA, herein designated VGAM RNA, and which when bound by VGAM1570 RNA causes inhibition of translation of respective one or more VGAM1570 host target proteins.

[53677] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1570 gene, herein designated VGAM GENE, on one or more VGAM1570 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53678] It is yet further appreciated that a function of VGAM1570 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1570 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1570 correlate with, and may be deduced from, the identity of the host target genes which VGAM1570 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53679] Nucleotide sequences of the VGAM1570 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1570 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1570 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1570 are further described hereinbelow with reference to Table 1.

[53680] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1570 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1570 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[53681] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1570 gene, herein designated VGAM is inhibition of expression of VGAM1570 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1570 correlate with, and may be deduced from, the identity of the target genes which VGAM1570 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53682] Beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_018644) is a VGAM1570 host target gene. B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GAT1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2, designated SEQ ID:20714 and SEQ ID:27626 respectively, to the nucleotide sequence of VGAM1570 RNA, herein designated VGAM RNA, also designated SEQ ID:4281.

[53683] A function of VGAM1570 is therefore inhibition of Beta-

1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_018644). Accordingly, utilities of VGAM1570 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GAT1. LOC144667 (Accession XM\_096648) is another VGAM1570 host target gene. LOC144667 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144667, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144667 BINDING SITE, designated SEQ ID:40449, to the nucleotide sequence of VGAM1570 RNA, herein designated VGAM RNA, also designated SEQ ID:4281.

[53684] Another function of VGAM1570 is therefore inhibition of LOC144667 (Accession XM\_096648). Accordingly, utilities of VGAM1570 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144667. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1571 (VGAM1571) viral gene, which modulates expression of respective host target genes



thereof, the function and utility of which host target genes is known in the art.

[53685] VGAM1571 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1571 was detected is described hereinabove with reference to Figs. 1–8.

[53686] VGAM1571 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1571 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53687] VGAM1571 gene encodes a VGAM1571 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1571 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1571 precursor RNA is designated SEQ ID:1557, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1557 is located at position 4 relative to the genome of Rhopalosiphum Padi Virus.

[53688] VGAM1571 precursor RNA folds onto itself, forming VGAM1571 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53689] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1571 folded precursor RNA into VGAM1571 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1571 RNA is designated SEQ ID:4282, and is provided hereinbelow with reference to the sequence listing part.

[53690] VGAM1571 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1571 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1571 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53691] VGAM1571 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1571 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1571 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1571 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1571 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53692] The complementary binding of VGAM1571 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1571 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1571 host target RNA into VGAM1571 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53693] It is appreciated that VGAM1571 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1571 host target genes. The mRNA of each one of this plurality of VGAM1571 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1571 RNA, herein designated VGAM RNA, and which when bound by VGAM1571 RNA causes inhibition of translation of respective one or more VGAM1571 host target proteins.

[53694] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1571 gene, herein designated VGAM GENE, on one or more VGAM1571 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53695] It is yet further appreciated that a function of VGAM1571 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGAM1571 correlate with, and may be deduced from, the identity of the host target genes which VGAM1571 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[53696] Nucleotide sequences of the VGAM1571 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1571 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1571 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1571 are further described hereinbelow with reference to Table 1.

[53697] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1571 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1571 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53698] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1571 gene, herein designated VGAM is inhibition of expression of VGAM1571 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1571 correlate with, and may be deduced from, the identity of the target genes which VGAM1571 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53699] Calmodulin 1 (phosphorylase kinase, delta) (CALM1, Accession NM\_006888) is a VGAM1571 host target gene. CALM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALM1 BINDING SITE, designated SEQ ID:13756, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53700] A function of VGAM1571 is therefore inhibition of Calmodulin 1 (phosphorylase kinase, delta) (CALM1, Accession NM\_006888), a gene which plays roles in growth and the cell cycle as well as in signal transduction and the synthesis and release of neurotransmitters. Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALM1. The function of CALM1 has been established by previous studies. Calmodulin is the archetype of the family of calcium-modulated proteins of which nearly 20 members have been found. They are identified by their occurrence in the cytosol or on membranes facing the cy-

tosol and by a high affinity for calcium. Calmodulin contains 149 amino acids and has 4 calcium-binding domains. Its functions include roles in growth and the cell cycle as well as in signal transduction and the synthesis and release of neurotransmitters. To determine how calcium/calmodulin activates calcium/calmodulin-dependent protein kinase I (CAMK1; 604998), Chin et al. (1997) characterized CAMK1 activation by calmodulin mutants with substitutions at hydrophobic residues. They found that CAMK1 activity is dependent on met124 within the C-terminal domain of calmodulin as well as on N-terminal hydrophobic residues of calmodulin.

[53701] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53702] Rhyner, J. A.; Ottiger, M.; Wicki, R.; Greenwood, T. M.; Strehler, E. E. : Structure of the human CALM1 calmodulin gene and identification of two CALM1-related pseudogenes CALM1P1 and CALM1P2. *Europ. J. Biochem.* 225: 71-82, 1994. ; and

[53703] Chin, D.; Winkler, K. E.; Means, A. R. : Characterization of substrate phosphorylation and use of calmodulin mutants to address implications from the enzyme crystal structure



of calmodul.

[53704] Further studies establishing the function and utilities of CALM1 are found in John Hopkins OMIM database record ID 114180, and in cited publications numbered 12573–1258 and 2 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fibronectin Leucine Rich Transmembrane Protein 3 (FLRT3, Accession NM\_013281) is another VGAM1571 host target gene. FLRT3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLRT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT3 BINDING SITE, designated SEQ ID:14948, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53705] Another function of VGAM1571 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 3 (FLRT3, Accession NM\_013281). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT3. Phosphoinositide-3-kinase, Regulatory Subunit, Polypep-

ptide 2 (p85 beta) (PIK3R2, Accession NM\_005027) is another VGAM1571 host target gene. PIK3R2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3R2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3R2 BINDING SITE, designated SEQ ID:11468, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53706] Another function of VGAM1571 is therefore inhibition of Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 2 (p85 beta) (PIK3R2, Accession NM\_005027), a gene which acts as an adapter and is regulatory subunit (p85 beta) of phosphatidylinositol 3-kinase. Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3R2. The function of PIK3R2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM647. Protein Kinase, CGMP-dependent, Type I (PRKG1, Accession NM\_006258) is another VGAM1571 host target gene. PRKG1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKG1 BINDING SITE, designated SEQ ID:12938, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53707] Another function of VGAM1571 is therefore inhibition of Protein Kinase, CGMP-dependent, Type I (PRKG1, Accession NM\_006258), a gene which relaxes vascular smooth muscle and inhibits platelet aggregation. Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKG1. The function of PRKG1 has been established by previous studies. Cyclic GMP and cyclic GMP-dependent protein kinase play important roles in physiologic processes such as relaxation of vascular smooth muscle and inhibition of platelet aggregation. Two main forms of cGK have been identified: a soluble form designated type I and an intrinsic membrane-bound form designated type II. Sandberg et al. (1989) isolated and characterized cDNA clones for the type I beta isozyme from human placenta

libraries. The same group used a genomic probe for mapping the gene (Orstavik et al., 1992). By Southern blots of human/hamster somatic cell hybrids, they localized the PRKGR1B gene to chromosome 10. The gene was regionally localized to 10q11.2 by in situ hybridization. Tamura et al. (1996) cloned a human cGKI- $\alpha$  cDNA by RT-PCR of aorta RNA using primers based on the sequence of a bovine cGKI- $\alpha$  cDNA. The predicted 671-amino acid human cGKI- $\alpha$  protein is nearly identical to bovine cGKI- $\alpha$ . Based on Southern blot and sequence analyses, Tamura et al. (1996) suggested that cGKI- $\alpha$  and cGKI- $\beta$  are generated by alternative splicing of a single gene that maps to chromosome 10. By Northern blot analysis, cGKI- $\alpha$  was abundantly expressed as a 7.0-kb mRNA in aorta, heart, kidneys and adrenals; the 7.0-kb cGKI- $\beta$  mRNA was abundantly expressed only in the uterus. Orstavik et al. (1997) noted that type I cGK is a homodimer, with each monomer containing a regulatory cGMP-binding domain and a catalytic domain. They reported that the type I cGK gene consists of 19 exons spanning at least 220 kb. The first 2 exons, which the authors called 1- $\alpha$  and 1- $\beta$ , are used alternatively and encode the  $\alpha$  isoform- and  $\beta$  isoform-specific

sequences. By Northern blot analysis, type I cGK- $\alpha$  mRNA was most abundant in lung and placenta, while type I cGK- $\beta$  was expressed at highest levels in bladder, uterus, adrenal gland, and fallopian tube. Orstavik et al. (1997) noted that 5 of the 7 splice sites in the *Drosophila melanogaster* DG2 gene, which encodes a cGK, are also present in the human type I cGK gene. Osborne et al. (1997) reported that levels of the DG2-encoded cGK in *Drosophila* affect food-search behavior and account for a naturally occurring behavioral polymorphism. Animal model experiments lend further support to the function of PRKG1. Pfeifer et al. (1998) generated mice deficient in cGKI by targeted disruption. Loss of cGKI abolished nitric oxide/cGMP-dependent relaxation of smooth muscle, resulting in severe vascular and intestinal dysfunction. However, cGKI-deficient smooth muscle responded normally to cAMP, indicating that cAMP and cGMP signal via independent pathways, with cGKI being the specific mediator of the nitric oxide/cGMP effects in murine smooth muscle.

[53708] It is appreciated that the abovementioned animal model for PRKG1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[53709] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53710] Pfeifer, A.; Klatt, P.; Massberg, S.; Ny, L.; Sausbier, M.; Hirneill, C.; Wang, G.-X.; Korth, M.; Aszodi, A.; Andersson, K.-E.; Krombach, F.; Mayerhofer, A.; Ruth, P.; Fassler, R.; Hofmann, F. : Defective smooth muscle regulation in cGMP kinase I-deficient mice. EMBO J. 17: 3045-3051, 1998. ; and

[53711] Sandberg, M.; Natarajan, V.; Ronander, I.; Kalderon, D.; Walter, U.; Lohmann, S. M.; Jahnsen, T. : Molecular cloning and predicted full-length amino acid sequence of the type I beta isoz.

[53712] Further studies establishing the function and utilities of PRKG1 are found in John Hopkins OMIM database record ID 176894, and in cited publications numbered 1148-1153 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAB23, Member RAS Oncogene Family (RAB23, Accession NM\_016277) is another VGAM1571 host target gene. RAB23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB23, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB23 BINDING SITE, designated SEQ ID:18402, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53713] Another function of VGAM1571 is therefore inhibition of RAB23, Member RAS Oncogene Family (RAB23, Accession NM\_016277), a gene which is involved in the regulation of intracellular membrane trafficking. Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB23. The function of RAB23 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340. Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM\_024331) is another VGAM1571 host target gene. C20orf121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf121 BINDING

SITE, designated SEQ ID:23636, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53714] Another function of VGAM1571 is therefore inhibition of Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM\_024331). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf121. FLJ22021 (Accession NM\_024535) is another VGAM1571 host target gene. FLJ22021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22021 BINDING SITE, designated SEQ ID:23746, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53715] Another function of VGAM1571 is therefore inhibition of FLJ22021 (Accession NM\_024535). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22021. KIAA0265 (Accession XM\_045954) is another



VGAM1571 host target gene. KIAA0265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0265 BINDING SITE, designated SEQ ID:34630, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53716] Another function of VGAM1571 is therefore inhibition of KIAA0265 (Accession XM\_045954). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0265. KIAA1483 (Accession XM\_045920) is another VGAM1571 host target gene. KIAA1483 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1483, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1483 BINDING SITE, designated SEQ ID:34616, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53717] Another function of VGAM1571 is therefore inhibition of KIAA1483 (Accession XM\_045920). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1483. KIAA1795 (Accession XM\_050988) is another VGAM1571 host target gene. KIAA1795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1795 BINDING SITE, designated SEQ ID:35700, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53718] Another function of VGAM1571 is therefore inhibition of KIAA1795 (Accession XM\_050988). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1795. MGC13061 (Accession NM\_032322) is another VGAM1571 host target gene. MGC13061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13061, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13061 BINDING SITE, designated SEQ ID:26131, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53719] Another function of VGAM1571 is therefore inhibition of MGC13061 (Accession NM\_032322). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13061. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM\_018450) is another VGAM1571 host target gene. SMARCF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMARCF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCF1 BINDING SITE, designated SEQ ID:20524, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53720] Another function of VGAM1571 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent

Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM\_018450). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCF1. Translocase of Inner Mitochondrial Membrane 9 Homolog (yeast) (TIMM9, Accession NM\_012460) is another VGAM1571 host target gene. TIMM9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TIMM9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIMM9 BINDING SITE, designated SEQ ID:14833, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53721] Another function of VGAM1571 is therefore inhibition of Translocase of Inner Mitochondrial Membrane 9 Homolog (yeast) (TIMM9, Accession NM\_012460). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIMM9. LOC143308 (Accession XM\_096411) is another VGAM1571 host target gene. LOC143308 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC143308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143308 BINDING SITE, designated SEQ ID:40348, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53722] Another function of VGAM1571 is therefore inhibition of LOC143308 (Accession XM\_096411). Accordingly, utilities of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143308. LOC51619 (Accession NM\_015983) is another VGAM1571 host target gene. LOC51619 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51619 BINDING SITE, designated SEQ ID:18078, to the nucleotide sequence of VGAM1571 RNA, herein designated VGAM RNA, also designated SEQ ID:4282.

[53723] Another function of VGAM1571 is therefore inhibition of LOC51619 (Accession NM\_015983). Accordingly, utilities

of VGAM1571 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51619. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1572 (VGAM1572) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53724] VGAM1572 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1572 was detected is described hereinabove with reference to Figs. 1-8.

[53725] VGAM1572 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1572 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53726] VGAM1572 gene encodes a VGAM1572 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1572 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1572 precursor RNA is designated SEQ ID:1558, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1558 is located at position 3435 relative to the genome of Rhopalosiphum Padi Virus.

[53727] VGAM1572 precursor RNA folds onto itself, forming VGAM1572 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53728] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1572 folded precursor RNA into VGAM1572 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1572 RNA is designated SEQ ID:4283, and

is provided hereinbelow with reference to the sequence listing part.

[53729] VGAM1572 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1572 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1572 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53730] VGAM1572 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1572 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1572 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-



ing – VGAM1572 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1572 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53731] The complementary binding of VGAM1572 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1572 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1572 host target RNA into VGAM1572 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53732] It is appreciated that VGAM1572 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1572 host target genes. The mRNA of each one of this plurality of VGAM1572 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1572 RNA, herein designated VGAM RNA, and which when bound by VGAM1572 RNA causes inhibition of translation of respective one or more VGAM1572 host target proteins.

[53733] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1572 gene, herein designated VGAM GENE, on one or more VGAM1572 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53734] It is yet further appreciated that a function of VGAM1572 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1572 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGAM1572 correlate with, and may be deduced from, the identity of the host target genes which VGAM1572 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53735] Nucleotide sequences of the VGAM1572 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1572 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1572 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1572 are further described hereinbelow with reference to Table 1.

[53736] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1572 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1572 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53737] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1572 gene, herein designated VGAM is inhibition of expression of VGAM1572 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1572 correlate with, and may be deduced from, the identity of the target genes which VGAM1572 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53738] FLJ13052 (Accession NM\_023018) is a VGAM1572 host target gene. FLJ13052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13052 BINDING SITE, designated SEQ ID:23285, to the nucleotide sequence of VGAM1572 RNA, herein designated VGAM RNA, also designated SEQ ID:4283.

[53739] A function of VGAM1572 is therefore inhibition of FLJ13052 (Accession NM\_023018). Accordingly, utilities of VGAM1572 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13052. KIAA0976 (Accession NM\_014917) is another VGAM1572 host target gene. KIAA0976 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0976 BINDING SITE, designated SEQ ID:17161, to the nucleotide sequence of VGAM1572 RNA, herein designated VGAM RNA, also designated SEQ ID:4283.

[53740] Another function of VGAM1572 is therefore inhibition of KIAA0976 (Accession NM\_014917). Accordingly, utilities of VGAM1572 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0976. KIAA1387 (Accession XM\_048092) is another VGAM1572 host target gene. KIAA1387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1387 BINDING SITE, designated SEQ ID:35104, to the nucleotide sequence of VGAM1572 RNA, herein designated VGAM RNA, also designated SEQ ID:4283.

[53741] Another function of VGAM1572 is therefore inhibition of

KIAA1387 (Accession XM\_048092). Accordingly, utilities of VGAM1572 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1387. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1573 (VGAM1573) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53742] VGAM1573 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1573 was detected is described hereinabove with reference to Figs. 1-8.

[53743] VGAM1573 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1573 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53744] VGAM1573 gene encodes a VGAM1573 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1573 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1573 precursor RNA is designated SEQ ID:1559, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1559 is located at position 3711 relative to the genome of Rhopalosiphum Padi Virus.

- [53745] VGAM1573 precursor RNA folds onto itself, forming VGAM1573 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [53746] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1573 folded precursor RNA into VGAM1573 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide se-

quence of VGAM1573 RNA is designated SEQ ID:4284, and is provided hereinbelow with reference to the sequence listing part.

[53747] VGAM1573 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1573 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1573 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53748] VGAM1573 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1573 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1573 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is



meant as an illustration only, and is not meant to be limiting – VGAM1573 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1573 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[53749] The complementary binding of VGAM1573 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1573 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1573 host target RNA into VGAM1573 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53750] It is appreciated that VGAM1573 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1573 host target genes. The mRNA of each one of this plurality of VGAM1573 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1573 RNA, herein designated VGAM RNA, and which when bound by VGAM1573 RNA causes inhibition of translation of respective one or more VGAM1573 host target proteins.

[53751] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1573 gene, herein designated VGAM GENE, on one or more VGAM1573 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53752] It is yet further appreciated that a function of VGAM1573

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1573 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGAM1573 correlate with, and may be deduced from, the identity of the host target genes which VGAM1573 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53753] Nucleotide sequences of the VGAM1573 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1573 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1573 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1573 are further described hereinbelow with reference to Table 1.

[53754] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1573 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1573 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53755] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1573 gene, herein designated VGAM is inhibition of expression of VGAM1573 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1573 correlate with, and may be deduced from, the identity of the target genes which VGAM1573 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53756] Cell Division Cycle 25A (CDC25A, Accession NM\_001789) is a VGAM1573 host target gene. CDC25A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDC25A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC25A BINDING SITE, designated SEQ ID:7540, to the nucleotide sequence of VGAM1573 RNA, herein designated VGAM RNA, also designated SEQ ID:4284.

[53757] A function of VGAM1573 is therefore inhibition of Cell Division Cycle 25A (CDC25A, Accession NM\_001789), a gene which is a tyrosine protein phosphatase required for progression of the cell cycle. Accordingly, utilities of VGAM1573 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CDC25A. The function of CDC25A has been established by previous studies. When exposed to ionizing radiation, eukaryotic cells activate checkpoint pathways to delay the progression of the cell cycle. Defects in the ionizing radiation-induced S-phase checkpoint cause 'radioresistant DNA synthesis,' a phenomenon that has been identified in cancer-prone patients suffering from ataxia-telangiectasia. The CDC25A phosphatase activates CDK2, needed for DNA synthesis, but becomes degraded in response to DNA damage or stalled replication. Falck et al. (2001) reported a functional link between ATM (OMIM Ref. No. 208900), checkpoint signaling kinase CHK2 (OMIM Ref. No. 604373), and CDC25A, and implicated this mechanism in controlling the S-phase checkpoint. Falck et al. (2001) showed that ionizing radiation-induced destruction of CDC25A requires both ATM and the CHK2-mediated phosphorylation of CDC25A on serine-123. An ionizing radiation-induced loss of CDC25A protein prevents dephosphorylation of CDK2 and leads to a transient blockade of DNA replication. Falck et al. (2001) also showed that tumor-associated CHK2 alleles cannot bind or phosphorylate CDC25A, and that cells expressing

these CHK2 alleles, elevated CDC25A, or a CDK2 mutant unable to undergo inhibitory phosphorylation (OMIM Ref. No. CDK2AF) fail to inhibit DNA synthesis when irradiated. Falck et al. (2001) concluded that their results support CHK2 as a candidate tumor suppressor, and identify the ATM--CHK2--CDC25A--CDK2 pathway as a genomic integrity checkpoint that prevents radioresistant DNA synthesis. Falck et al. (2002) demonstrated that experimental blockade of either the NBS1 (OMIM Ref. No. 602667)--MRE11 (OMIM Ref. No. 600814) function or the CHK2-triggered events leads to a partial radioresistant DNA synthesis phenotype in human cells. In contrast, concomitant interference with NBS1-MRE11 and the CHK2-CDC25A-CDK2 pathways entirely abolishes inhibition of DNA synthesis induced by ionizing radiation, resulting in complete radioresistant DNA synthesis analogous to that caused by defective ATM. In addition, CDK2-dependent loading of CDC45 (OMIM Ref. No. 603465) onto replication origins, a prerequisite for recruitment of DNA polymerase, was prevented upon irradiation of normal or NBS1/MRE11-defective cells but not cells with defective ATM. Falck et al. (2002) concluded that in response to ionizing radiation, phosphorylation of

NBS1 and CHK2 by ATM triggers 2 parallel branches of the DNA damage–dependent S–phase checkpoint that cooperate by inhibiting distinct steps of DNA replication. To protect genome integrity and ensure survival, eukaryotic cells exposed to genotoxic stress cease proliferating to provide time for DNA repair. Mailand et al. (2000) demonstrated that human cells respond to ultraviolet light or ionizing radiation by rapid, ubiquitin– and proteasome–dependent protein degradation of CDC25A, a phosphatase that is required for progression from G1 to S phase of the cell cycle. This response involved activated CHK1 protein kinase (OMIM Ref. No. 603078) but not the p53 (OMIM Ref. No. 191170) pathway, and the persisting inhibitory tyrosine phosphorylation of CDK2 (OMIM Ref. No. 116953) blocked entry into S phase and DNA replication.

CDC25A–dependent cell cycle arrest occurs 1 to 2 hours after ultraviolet radiation, whereas the p53–p21 axis affects the cell cycle only several hours after ultraviolet treatment. Mailand et al. (2000) thus concluded that the checkpoint response to DNA damage occurs in 2 waves. Overexpression of CDC25A bypassed the mechanism of cell cycle arrest, leading to enhanced DNA damage and decreased cell survival. Mailand et al. (2000) concluded

that the results identified specific degradation of CDC25A as part of the DNA damage checkpoint mechanism and suggested how CDC25A overexpression in human cancers might contribute to tumorigenesis.

[53758] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53759] Mailand, N.; Falck, J.; Lukas, C.; Syljuasen, R. G.; Welcker, M.; Bartek, J.; Lukas, J. : Rapid destruction of human Cdc25A in response to DNA damage. Science 288: 1425–1429, 2000. ; and

[53760] Falck, J.; Mailand, N.; Syljuasen, R. G.; Bartek, J.; Lukas, J. : The ATM–Chk2–Cdc25A checkpoint pathway guards against radioresistant DNA synthesis. Nature 410: 842–847, 2001.

[53761] Further studies establishing the function and utilities of CDC25A are found in John Hopkins OMIM database record ID 116947, and in cited publications numbered 1932–149 and 1933–1935 listed in the bibliography section herein–below, which are also hereby incorporated by reference. GRAF (Accession NM\_015071) is another VGAM1573 host target gene. GRAF BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA



encoded by GRAF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRAF BINDING SITE, designated SEQ ID:17442, to the nucleotide sequence of VGAM1573 RNA, herein designated VGAM RNA, also designated SEQ ID:4284.

[53762] Another function of VGAM1573 is therefore inhibition of GRAF (Accession NM\_015071), a gene which is a GTPase activating protein for p21-rac. Accordingly, utilities of VGAM1573 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRAF. The function of GRAF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430. Potassium Voltage-gated Channel, Subfamily H (eag-related), Member 2 (KCNH2, Accession NM\_000238) is another VGAM1573 host target gene. KCNH2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of KCNH2 BINDING SITE, designated SEQ ID:5755, to the nucleotide sequence of VGAM1573 RNA, herein designated VGAM RNA, also designated SEQ ID:4284.

[53763] Another function of VGAM1573 is therefore inhibition of Potassium Voltage-gated Channel, Subfamily H (eag-related), Member 2 (KCNH2, Accession NM\_000238), a gene which inwardly rectifying cardiac potassium (ikr) channel. Accordingly, utilities of VGAM1573 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNH2. The function of KCNH2 has been established by previous studies. Sanguinetti et al. (1995) expressed the HERG gene in *Xenopus laevis* oocytes and studied the potassium channel's biophysical properties and its sensitivity to various pharmacological agents. Their data indicated that HERG proteins form I(Kr) channels, but that another subunit may be required for certain drug sensitivities. Since block of I(Kr) is a known mechanism for drug-induced cardiac arrhythmias, their findings provided a mechanistic link between certain types of inherited and acquired LQT. Acquired long QT syndrome occurs following treatment with certain medications and in association with reduced serum potassium

levels (hypokalemia). Both acquired and inherited LQTS are associated with torsade de pointes and polymorphic ventricular tachycardia resulting from abnormal cardiac depolarization (as detected by QT prolongation on the electrocardiogram). LQT is also characterized by sinusoidal twisting of the QRS axis around the isoelectric line. Torsade de pointes can degenerate into ventricular fibrillation, which can lead to sudden death Li et al. (1997) identified a subunit interaction domain, termed the NAB domain, in the hydrophilic cytoplasmic N terminus of HERG. This domain is responsible for the oligomerization of the protein into functional tetramers. Truncated HERG proteins, including the deletion mutant at position 1261 (152427.0007), contain the NAB domain but lack the rest of the channel and thus inhibit the expression of functional tetrameric HERG channels in transfected cells. The authors suggested that LQT may be the result of decreased expression of a functional HERG potassium channel in the heart.

[53764] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53765] Priori, S. G.; Napolitano, C.; Schwartz, P. J. : Low pene-

trance in the long QT syndrome: clinical impact. Circulation 99: 529–533, 1999. ; and

[53766] Rajamani, S.; Anderson, C. L.; Anson, B. D.; January, C. T. : Pharmacological rescue of human K<sup>+</sup> channel long-QT2 mutations. Circulation 105: 2830–2835, 2002.

[53767] Further studies establishing the function and utilities of KCNH2 are found in John Hopkins OMIM database record ID 152427, and in cited publications numbered 3435, 354 and 2198–2223 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Diacylglycerol Kinase, Delta 130kDa (DGKD, Accession XM\_002384) is another VGAM1573 host target gene. DGKD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGKD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKD BINDING SITE, designated SEQ ID:29881, to the nucleotide sequence of VGAM1573 RNA, herein designated VGAM RNA, also designated SEQ ID:4284.

[53768] Another function of VGAM1573 is therefore inhibition of Diacylglycerol Kinase, Delta 130kDa (DGKD, Accession XM\_002384). Accordingly, utilities of VGAM1573 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKD. FLJ12484 (Accession XM\_045681) is another VGAM1573 host target gene.

FLJ12484 BINDING SITE1 and FLJ12484 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ12484, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12484 BINDING SITE1 and FLJ12484 BINDING SITE2, designated SEQ ID:34516 and SEQ ID:23018 respectively, to the nucleotide sequence of VGAM1573 RNA, herein designated VGAM RNA, also designated SEQ ID:4284.

[53769] Another function of VGAM1573 is therefore inhibition of FLJ12484 (Accession XM\_045681). Accordingly, utilities of VGAM1573 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12484. MGC1842 (Accession XM\_037797) is another VGAM1573 host target gene. MGC1842 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC1842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC1842 BINDING SITE, designated SEQ ID:32687, to the nucleotide sequence of VGAM1573 RNA, herein designated VGAM RNA, also designated SEQ ID:4284.

[53770] Another function of VGAM1573 is therefore inhibition of MGC1842 (Accession XM\_037797). Accordingly, utilities of VGAM1573 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC1842. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1574 (VGAM1574) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53771] VGAM1574 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1574 was detected is described hereinabove with reference to Figs. 1–8.

[53772] VGAM1574 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1574 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[53773] VGAM1574 gene encodes a VGAM1574 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1574 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1574 precursor RNA is designated SEQ ID:1560, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1560 is located at position 7836 relative to the genome of Rhopalosiphum Padi Virus.

[53774] VGAM1574 precursor RNA folds onto itself, forming VGAM1574 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53775] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1574 folded precursor RNA into VGAM1574 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1574 RNA is designated SEQ ID:4285, and is provided hereinbelow with reference to the sequence listing part.

[53776] VGAM1574 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1574 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1574 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53777] VGAM1574 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1574 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1574 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-



quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1574 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1574 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53778] The complementary binding of VGAM1574 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1574 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1574 host target RNA into VGAM1574 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53779] It is appreciated that VGAM1574 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1574 host target genes. The mRNA of each one of this plurality of VGAM1574 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1574 RNA, herein designated VGAM RNA, and which when bound by VGAM1574 RNA causes inhibition of translation of respective one or more VGAM1574 host target proteins.

[53780] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1574 gene, herein designated VGAM GENE, on one or more VGAM1574 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53781] It is yet further appreciated that a function of VGAM1574 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1574 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGAM1574 correlate with, and may be deduced from, the identity of the host target genes which VGAM1574 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53782] Nucleotide sequences of the VGAM1574 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1574 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1574 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1574 are further described hereinbelow with reference to Table 1.

[53783] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1574 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1574 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53784] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1574 gene, herein designated VGAM is inhibition of expression of VGAM1574 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1574 correlate with, and may be deduced from, the identity of the target genes which VGAM1574 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53785] Dipeptidase 1 (renal) (DPEP1, Accession NM\_004413) is a VGAM1574 host target gene. DPEP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DPEP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPEP1 BINDING SITE, designated SEQ ID:10674, to the nucleotide sequence of VGAM1574 RNA, herein designated VGAM RNA, also designated SEQ ID:4285.

[53786] A function of VGAM1574 is therefore inhibition of Dipeptidase 1 (renal) (DPEP1, Accession NM\_004413), a gene which hydrolyzes a wide range of dipeptides. Accordingly, utilities of VGAM1574 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPEP1. The function of DPEP1 has been established by previous studies. Renal dipeptidase, previously referred to as dehydropeptidase I or microsomal dipeptidase (MDP; EC 3.4.13.11), is a kidney membrane enzyme which hydrolyzes a variety of dipeptides and is implicated in the renal metabolism of glutathione and its conjugates, e.g., leukotriene D4 (Kozak and Tate, 1982). RDP is responsible for hydrolysis of the beta-lactam ring of antibiotics such as penem and carbapenem (Campbell et al., 1984). Earlier, beta-lactamase enzymes were thought to occur only in bacteria, where their probable function was in protecting the organisms against the action of beta-lactam antibiotics. These antibiotics exhibit selective toxicity against bacteria but virtual inertness against many eukaryotic cells. Adachi et al. (1990) isolated and characterized cDNA clones for human RDP. DNA and RNA blot analysis indicated the existence of a single gene. By fluorescence in situ hybridization (FISH), Nakagawa et al. (1991) mapped

the RDP gene to 16q24. To isolate potential tumor/growth suppressor genes involved in Wilms tumor, Austruy et al. (1993) constructed a cDNA library by cloning a mature kidney cDNA subtracted with an excess of Wilms tumor mRNA. Clones were selected according to a differential pattern of expression, i.e., positive with RNA from mature kidney and negative with RNA from several Wilms tumors. By comparison of sequences of these clones with the GENBANK database sequences, 1 clone was identified as renal dipeptidase (DPEP1), which had previously been mapped to 16q24 by in situ hybridization. Austruy et al. (1993) used somatic cell hybrids carrying either different human chromosomes or chromosome 16 segments to confirm and refine the physical mapping of DPEP1 to 16q24.3. Two RFLPs were described and used to show linkage of DPEP1 to D16S7; maximum lod score = 5.8 at theta = 0.03.

[53787] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53788] Austruy, E.; Jeanpierre, C.; Antignac, C.; Whitmore, S. A.; Van Cong, N.; Bernheim, A.; Callen, D. F.; Junien, C. : Physical and genetic mapping of the dipeptidase gene

- DPEP1 to 16q24.3. Genomics 15: 684–687, 1993. ; and
- [53789] Nakagawa, H.; Inazawa, J.; Inoue, K.; Misawa, S.; Kashima, K.; Adachi, H.; Nakazato, H.; Abe, T. : Assignment of the human renal dipeptidase gene (DPEP1) to band q24 of chromosome 16. (A.
- [53790] Further studies establishing the function and utilities of DPEP1 are found in John Hopkins OMIM database record ID 179780, and in cited publications numbered 1555–1559 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM\_002006) is another VGAM1574 host target gene. FGF2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF2 BINDING SITE, designated SEQ ID:7733, to the nucleotide sequence of VGAM1574 RNA, herein designated VGAM RNA, also designated SEQ ID:4285.
- [53791] Another function of VGAM1574 is therefore inhibition of Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM\_002006), a gene which probably involved in nervous

system development and function. Accordingly, utilities of VGAM1574 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF2. The function of FGF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51. KIAA0172 (Accession XM\_036295) is another VGAM1574 host target gene. KIAA0172 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0172 BINDING SITE, designated SEQ ID:32411, to the nucleotide sequence of VGAM1574 RNA, herein designated VGAM RNA, also designated SEQ ID:4285.

[53792] Another function of VGAM1574 is therefore inhibition of KIAA0172 (Accession XM\_036295). Accordingly, utilities of VGAM1574 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0172. KIAA0316 (Accession XM\_045712) is another VGAM1574 host target gene. KIAA0316 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by KIAA0316, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0316 BINDING SITE, designated SEQ ID:34530, to the nucleotide sequence of VGAM1574 RNA, herein designated VGAM RNA, also designated SEQ ID:4285.

[53793] Another function of VGAM1574 is therefore inhibition of KIAA0316 (Accession XM\_045712). Accordingly, utilities of VGAM1574 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0316. KIAA0483 (Accession NM\_015176) is another VGAM1574 host target gene. KIAA0483 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0483, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0483 BINDING SITE, designated SEQ ID:17528, to the nucleotide sequence of VGAM1574 RNA, herein designated VGAM RNA, also designated SEQ ID:4285.

[53794] Another function of VGAM1574 is therefore inhibition of KIAA0483 (Accession NM\_015176). Accordingly, utilities

of VGAM1574 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0483. KIAA1538 (Accession XM\_049474) is another VGAM1574 host target gene. KIAA1538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1538 BINDING SITE, designated SEQ ID:35425, to the nucleotide sequence of VGAM1574 RNA, herein designated VGAM RNA, also designated SEQ ID:4285.

[53795] Another function of VGAM1574 is therefore inhibition of KIAA1538 (Accession XM\_049474). Accordingly, utilities of VGAM1574 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1538. LOC133088 (Accession XM\_059624) is another VGAM1574 host target gene. LOC133088 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC133088, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC133088 BINDING SITE, designated SEQ ID:37033, to the nucleotide sequence of VGAM1574 RNA, herein designated VGAM RNA, also designated SEQ ID:4285.

[53796] Another function of VGAM1574 is therefore inhibition of LOC133088 (Accession XM\_059624). Accordingly, utilities of VGAM1574 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133088. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1575 (VGAM1575) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53797] VGAM1575 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1575 was detected is described hereinabove with reference to Figs. 1–8.

[53798] VGAM1575 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1575 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53799] VGAM1575 gene encodes a VGAM1575 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1575 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1575 precursor RNA is designated SEQ ID:1561, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1561 is located at position 923 relative to the genome of Rhopalosiphum Padi Virus.

[53800] VGAM1575 precursor RNA folds onto itself, forming VGAM1575 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53801] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1575 folded precursor RNA into VGAM1575 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1575 RNA is designated SEQ ID:4286, and is provided hereinbelow with reference to the sequence listing part.

[53802] VGAM1575 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1575 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1575 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53803] VGAM1575 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1575 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1575 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1575 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1575 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53804] The complementary binding of VGAM1575 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1575 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1575 host target RNA into VGAM1575 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53805] It is appreciated that VGAM1575 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1575 host target genes. The mRNA of each one of this plurality of VGAM1575 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1575 RNA, herein designated VGAM RNA, and which when bound by VGAM1575 RNA causes inhibition of translation of respective one or more VGAM1575 host target proteins.

[53806] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1575 gene, herein designated VGAM GENE, on one or more VGAM1575 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[53807] It is yet further appreciated that a function of VGAM1575 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGAM1575 correlate with, and may be deduced from, the identity of the host target genes which VGAM1575 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53808] Nucleotide sequences of the VGAM1575 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1575 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1575 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1575 are further described hereinbelow with reference to Table 1.

[53809] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1575 host target RNA, and



schematic representation of the complementarity of each of these host target binding sites to VGAM1575 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53810] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1575 gene, herein designated VGAM is inhibition of expression of VGAM1575 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1575 correlate with, and may be deduced from, the identity of the target genes which VGAM1575 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53811] FAT Tumor Suppressor Homolog 2 (Drosophila) (FAT2, Accession NM\_001447) is a VGAM1575 host target gene. FAT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FAT2 BINDING SITE, designated SEQ ID:7173, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53812] A function of VGAM1575 is therefore inhibition of FAT

Tumor Suppressor Homolog 2 (Drosophila) (FAT2, Accession NM\_001447), a gene which could function as a cell-adhesion protein. Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAT2. The function of FAT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM949. Glycosylphosphatidylinositol Specific Phospholipase D1 (GPLD1, Accession XM\_166347) is another VGAM1575 host target gene. GPLD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPLD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPLD1 BINDING SITE, designated SEQ ID:44180, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53813] Another function of VGAM1575 is therefore inhibition of Glycosylphosphatidylinositol Specific Phospholipase D1 (GPLD1, Accession XM\_166347), a gene which hydrolyses the inositol phosphate linkage in proteins anchored by

phosphatidylinositol glycans to release these proteins from the membrane. Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPLD1. The function of GPLD1 has been established by previous studies. Many proteins are attached to the plasma membrane via a glycosylphosphatidylinositol (GPI) anchor. Phosphatidylinositol-glycan (PIG)-specific phospholipases D (PLDs) selectively hydrolyze the inositol phosphate linkage, allowing release of the protein. Scallan et al. (1991) cloned a cDNA encoding a PIGPLD from a bovine liver cDNA library. The deduced amino acid sequence contains 4 regions of internal homology that are similar to the metal ion binding domains of integrin alpha subunits (see OMIM Ref. No. ITGA2, 192974). Bovine PIGPLD does not exhibit phosphatidylcholine-specific PLD (OMIM Ref. No. 602382) activity. By PCR and screening of a human liver cDNA library, Tsang et al. (1992) isolated a cDNA (OMIM Ref. No. L11701) encoding a PIGPLD. The protein product contains 841 amino acids, including a 24-residue signal sequence. Tsang et al. (1992) isolated a cDNA (OMIM Ref. No. L11702) encoding a related but distinct PIGPLD from a human pancreas cDNA library. The pancreas-derived PIG-

PLD contains 840 amino acids, including a 23-residue signal sequence. Schofield and Rademacher (2000) determined that the GPLD1 gene contains 25 exons and spans at least 80 kb. Northern blot analysis revealed expression of 5.8-kb transcript that was restricted to liver. Southern blot analysis indicated that GPLD1 is a single-copy gene.

[53814] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[53815] Schofield, J. N.; Rademacher, T. W. : Structure and expression of the human glycosylphosphatidylinositol phospholipase D1 (GPLD1) gene. *Biochim. Biophys. Acta* 1494: 189–194, 2000. ; and

[53816] Tsang, T. C.; Fung, W.-J.; Levine, J.; Metz, C. N.; Davitz, M. A.; Burns, D. K.; Huang, K.-S.; Kochan, J. P. : Isolation and expression of two human glycosylphosphatidylinositol phospho.

[53817] Further studies establishing the function and utilities of GPLD1 are found in John Hopkins OMIM database record ID 602515, and in cited publications numbered 8549–8552 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphodiesterase 4B, CAMP-specific

(phosphodiesterase E4 dunce homolog, *Drosophila*) (PDE4B, Accession NM\_002600) is another VGAM1575 host target gene. PDE4B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4B BINDING SITE, designated SEQ ID:8466, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53818] Another function of VGAM1575 is therefore inhibition of Phosphodiesterase 4B, CAMP-specific (phosphodiesterase E4 dunce homolog, *Drosophila*) (PDE4B, Accession NM\_002600), a gene which may be involved in mediating central nervous system effects of therapeutic agents ranging from antidepressants to antiasthmatic and anti-inflammatory agents. Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4B. The function of PDE4B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM51.Chromosome 20 Open Reading Frame 44 (C20orf44, Accession NM\_018244) is another VGAM1575 host target gene. C20orf44 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf44, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf44 BINDING SITE, designated SEQ ID:20207, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53819] Another function of VGAM1575 is therefore inhibition of Chromosome 20 Open Reading Frame 44 (C20orf44, Accession NM\_018244). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf44.

FLJ20445 (Accession NM\_017824) is another VGAM1575 host target gene. FLJ20445 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20445 BINDING SITE,

designated SEQ ID:19479, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53820] Another function of VGAM1575 is therefore inhibition of FLJ20445 (Accession NM\_017824). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20445. FLJ21034 (Accession NM\_024940) is another VGAM1575 host target gene. FLJ21034 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21034 BINDING SITE, designated SEQ ID:24483, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53821] Another function of VGAM1575 is therefore inhibition of FLJ21034 (Accession NM\_024940). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21034. KIAA1272 (Accession XM\_046600) is another VGAM1575 host target gene. KIAA1272 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1272, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1272 BINDING SITE, designated SEQ ID:34760, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53822] Another function of VGAM1575 is therefore inhibition of KIAA1272 (Accession XM\_046600). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1272. KIAA1911 (Accession XM\_056302) is another VGAM1575 host target gene. KIAA1911 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1911, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1911 BINDING SITE, designated SEQ ID:36393, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53823] Another function of VGAM1575 is therefore inhibition of



KIAA1911 (Accession XM\_056302). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1911. NCUBE1 (Accession NM\_016021) is another VGAM1575 host target gene. NCUBE1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCUBE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCUBE1 BINDING SITE, designated SEQ ID:18093, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53824] Another function of VGAM1575 is therefore inhibition of NCUBE1 (Accession NM\_016021). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCUBE1. SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM\_031469) is another VGAM1575 host target gene. SH3BGRL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL2, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL2 BINDING SITE, designated SEQ ID:25529, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53825] Another function of VGAM1575 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM\_031469). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BGRL2. ZIC4 (Accession NM\_032153) is another VGAM1575 host target gene. ZIC4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZIC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZIC4 BINDING SITE, designated SEQ ID:25853, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53826] Another function of VGAM1575 is therefore inhibition of ZIC4 (Accession NM\_032153). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ZIC4. LOC144017 (Accession XM\_096520) is another VGAM1575 host target gene. LOC144017 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144017 BINDING SITE, designated SEQ ID:40387, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53827] Another function of VGAM1575 is therefore inhibition of LOC144017 (Accession XM\_096520). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144017. LOC201689 (Accession XM\_040608) is another VGAM1575 host target gene. LOC201689 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC201689, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201689 BINDING SITE, designated SEQ ID:33334, to

the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53828] Another function of VGAM1575 is therefore inhibition of LOC201689 (Accession XM\_040608). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201689. LOC84549 (Accession NM\_032509) is another VGAM1575 host target gene. LOC84549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC84549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC84549 BINDING SITE, designated SEQ ID:26260, to the nucleotide sequence of VGAM1575 RNA, herein designated VGAM RNA, also designated SEQ ID:4286.

[53829] Another function of VGAM1575 is therefore inhibition of LOC84549 (Accession NM\_032509). Accordingly, utilities of VGAM1575 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC84549. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1576 (VGAM1576) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53830] VGAM1576 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1576 was detected is described hereinabove with reference to Figs. 1–8.

[53831] VGAM1576 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1576 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53832] VGAM1576 gene encodes a VGAM1576 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1576 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1576 precursor RNA is designated SEQ ID:1562, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1562 is located at position 3322 relative to the genome of Rhopalosiphum Padi Virus.

[53833] VGAM1576 precursor RNA folds onto itself, forming VGAM1576 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53834] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1576 folded precursor RNA into VGAM1576 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1576 RNA is designated SEQ ID:4287, and is provided hereinbelow with reference to the sequence listing part.

[53835] VGAM1576 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1576 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1576 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[53836] VGAM1576 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1576 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1576 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1576 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1576 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53837] The complementary binding of VGAM1576 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1576 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1576 host target RNA into VGAM1576 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53838] It is appreciated that VGAM1576 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1576 host target genes. The mRNA of each one of this plurality of VGAM1576 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1576 RNA, herein designated VGAM RNA, and which when bound by VGAM1576 RNA causes inhibition of translation of respective one or more VGAM1576 host target proteins.

[53839] It is further appreciated by one skilled in the art that the



mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1576 gene, herein designated VGAM GENE, on one or more VGAM1576 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53840] It is yet further appreciated that a function of VGAM1576 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1576 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGAM1576 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1576 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53841] Nucleotide sequences of the VGAM1576 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1576 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1576 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1576 are further described hereinbelow with reference to Table 1.

[53842] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1576 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1576 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53843] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1576 gene, herein designated VGAM is inhibition of expression of VGAM1576 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1576 correlate with, and may be deduced from, the identity of the target genes which VGAM1576

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53844] KIAA1350 (Accession XM\_052597) is a VGAM1576 host target gene. KIAA1350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1350 BINDING SITE, designated SEQ ID:36001, to the nucleotide sequence of VGAM1576 RNA, herein designated VGAM RNA, also designated SEQ ID:4287.

[53845] A function of VGAM1576 is therefore inhibition of KIAA1350 (Accession XM\_052597). Accordingly, utilities of VGAM1576 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1350. Protocadherin 10 (PCDH10, Accession NM\_020815) is another VGAM1576 host target gene. PCDH10 BINDING SITE1 and PCDH10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the comple-

mentarity of the nucleotide sequences of PCDH10 BINDING SITE1 and PCDH10 BINDING SITE2, designated SEQ ID:21884 and SEQ ID:26770 respectively, to the nucleotide sequence of VGAM1576 RNA, herein designated VGAM RNA, also designated SEQ ID:4287.

[53846] Another function of VGAM1576 is therefore inhibition of Protocadherin 10 (PCDH10, Accession NM\_020815). Accordingly, utilities of VGAM1576 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH10. TAF9-like RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 31kDa (TAF9L, Accession NM\_015975) is another VGAM1576 host target gene. TAF9L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAF9L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF9L BINDING SITE, designated SEQ ID:18073, to the nucleotide sequence of VGAM1576 RNA, herein designated VGAM RNA, also designated SEQ ID:4287.

[53847] Another function of VGAM1576 is therefore inhibition of TAF9-like RNA Polymerase II, TATA Box Binding Protein

(TBP)-associated Factor, 31kDa (TAF9L, Accession NM\_015975). Accordingly, utilities of VGAM1576 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF9L. Trans-golgi Network Protein 2 (TGOLN2, Accession XM\_034215) is another VGAM1576 host target gene. TGOLN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGOLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGOLN2 BINDING SITE, designated SEQ ID:32024, to the nucleotide sequence of VGAM1576 RNA, herein designated VGAM RNA, also designated SEQ ID:4287.

[53848] Another function of VGAM1576 is therefore inhibition of Trans-golgi Network Protein 2 (TGOLN2, Accession XM\_034215). Accordingly, utilities of VGAM1576 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGOLN2. LOC153364 (Accession XM\_087657) is another VGAM1576 host target gene. LOC153364 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153364, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153364 BINDING SITE, designated SEQ ID:39370, to the nucleotide sequence of VGAM1576 RNA, herein designated VGAM RNA, also designated SEQ ID:4287.

[53849] Another function of VGAM1576 is therefore inhibition of LOC153364 (Accession XM\_087657). Accordingly, utilities of VGAM1576 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153364. LOC155072 (Accession XM\_098661) is another VGAM1576 host target gene. LOC155072 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC155072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155072 BINDING SITE, designated SEQ ID:41761, to the nucleotide sequence of VGAM1576 RNA, herein designated VGAM RNA, also designated SEQ ID:4287.

[53850] Another function of VGAM1576 is therefore inhibition of LOC155072 (Accession XM\_098661). Accordingly, utilities of VGAM1576 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC155072. LOC202868 (Accession XM\_117477) is another VGAM1576 host target gene. LOC202868 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202868, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202868 BINDING SITE, designated SEQ ID:43448, to the nucleotide sequence of VGAM1576 RNA, herein designated VGAM RNA, also designated SEQ ID:4287.

[53851] Another function of VGAM1576 is therefore inhibition of LOC202868 (Accession XM\_117477). Accordingly, utilities of VGAM1576 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202868. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1577 (VGAM1577) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53852] VGAM1577 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1577 was detected is described hereinabove with reference to Figs. 1–8.

[53853] VGAM1577 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1577 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53854] VGAM1577 gene encodes a VGAM1577 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1577 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1577 precursor RNA is designated SEQ ID:1563, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1563 is located at position 2545 relative to the genome of Rhopalosiphum Padi Virus.

[53855] VGAM1577 precursor RNA folds onto itself, forming VGAM1577 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by



miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53856] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1577 folded precursor RNA into VGAM1577 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 90%) nucleotide sequence of VGAM1577 RNA is designated SEQ ID:4288, and is provided hereinbelow with reference to the sequence listing part.

[53857] VGAM1577 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1577 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1577 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53858] VGAM1577 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1577 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1577 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1577 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1577 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53859] The complementary binding of VGAM1577 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1577 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1577 host target RNA into VGAM1577 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53860] It is appreciated that VGAM1577 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1577 host target genes. The mRNA of each one of this plurality of VGAM1577 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1577 RNA, herein designated VGAM RNA, and which when bound by VGAM1577 RNA causes inhibition of translation of respective one or more VGAM1577 host target proteins.

[53861] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1577 gene, herein designated VGAM GENE, on one or more VGAM1577 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53862] It is yet further appreciated that a function of VGAM1577 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1577 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGAM1577 correlate with, and may be deduced from, the identity of the host target genes which VGAM1577 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53863] Nucleotide sequences of the VGAM1577 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1577 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1577 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1577 are further described hereinbelow with reference to Table 1.

[53864] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1577 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1577 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53865] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1577 gene, herein designated VGAM is inhibition of expression of VGAM1577 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1577 correlate with, and may be deduced from, the identity of the target genes which VGAM1577 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53866] Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM\_005228) is a VGAM1577 host target

gene. EGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFR BINDING SITE, designated SEQ ID:11724, to the nucleotide sequence of VGAM1577 RNA, herein designated VGAM RNA, also designated SEQ ID:4288.

[53867] A function of VGAM1577 is therefore inhibition of Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM\_005228), a gene which is a receptor for egf, but also for other members of the egf family. Accordingly, utilities of VGAM1577 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFR. The function of EGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229. Glutamate-ammonia Ligase (glutamine synthase) (GLUL, Accession NM\_002065) is another VGAM1577 host target gene. GLUL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLUL, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLUL BINDING SITE, designated SEQ ID:7833, to the nucleotide sequence of VGAM1577 RNA, herein designated VGAM RNA, also designated SEQ ID:4288.

[53868] Another function of VGAM1577 is therefore inhibition of Glutamate-ammonia Ligase (glutamine synthase) (GLUL, Accession NM\_002065), a gene which catalyzes the condensation of glutamate and ammonia to form glutamine. Accordingly, utilities of VGAM1577 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLUL. The function of GLUL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM948. SMUG1 (Accession NM\_014311) is another VGAM1577 host target gene. SMUG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMUG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMUG1 BINDING SITE, designated SEQ

ID:15608, to the nucleotide sequence of VGAM1577 RNA, herein designated VGAM RNA, also designated SEQ ID:4288.

[53869] Another function of VGAM1577 is therefore inhibition of SMUG1 (Accession NM\_014311). Accordingly, utilities of VGAM1577 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMUG1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1578 (VGAM1578) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53870] VGAM1578 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1578 was detected is described hereinabove with reference to Figs. 1–8.

[53871] VGAM1578 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1578 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53872] VGAM1578 gene encodes a VGAM1578 precursor RNA,



herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1578 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1578 precursor RNA is designated SEQ ID:1564, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1564 is located at position 3984 relative to the genome of Rhopalosiphum Padi Virus.

- [53873] VGAM1578 precursor RNA folds onto itself, forming VGAM1578 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [53874] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1578 folded precursor RNA into VGAM1578 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1578 RNA is designated SEQ ID:4289, and is provided hereinbelow with reference to the sequence listing part.

[53875] VGAM1578 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1578 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1578 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53876] VGAM1578 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1578 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1578 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1578 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1578 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53877] The complementary binding of VGAM1578 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1578 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1578 host target RNA into VGAM1578 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53878] It is appreciated that VGAM1578 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1578 host target genes. The mRNA of each one of this plurality of VGAM1578 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1578 RNA, herein designated VGAM RNA, and which when bound by VGAM1578 RNA causes inhibition of translation of respective one or more VGAM1578 host target proteins.

[53879] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1578 gene, herein designated VGAM GENE, on one or more VGAM1578 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[53880] It is yet further appreciated that a function of VGAM1578 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGAM1578 correlate with, and may be deduced from, the identity of the host target genes which VGAM1578 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53881] Nucleotide sequences of the VGAM1578 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1578 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1578 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1578 are further described hereinbelow with reference to Table 1.

[53882] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1578 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1578 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53883] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1578 gene, herein designated VGAM is inhibition of expression of VGAM1578 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1578 correlate with, and may be deduced from, the identity of the target genes which VGAM1578 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53884] Cyclin F (CCNF, Accession NM\_001761) is a VGAM1578 host target gene. CCNF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCNF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNF BINDING SITE, designated SEQ ID:7527, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53885] A function of VGAM1578 is therefore inhibition of Cyclin F (CCNF, Accession NM\_001761), a gene which likely to be

involved in the control of the cell cycle during s phase and g2. Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNF. The function of CCNF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM367. Cockayne Syndrome 1 (classical) (CKN1, Accession NM\_000082) is another VGAM1578 host target gene. CKN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKN1 BINDING SITE, designated SEQ ID:5531, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53886] Another function of VGAM1578 is therefore inhibition of Cockayne Syndrome 1 (classical) (CKN1, Accession NM\_000082). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKN1. Collagen, Type IV, Alpha 3 (Goodpasture antigen) (COL4A3, Accession

NM\_000091) is another VGAM1578 host target gene. COL4A3 BINDING SITE1 through COL4A3 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL4A3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A3 BINDING SITE1 through COL4A3 BINDING SITE3, designated SEQ ID:5549, SEQ ID:25356 and SEQ ID:25362 respectively, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53887] Another function of VGAM1578 is therefore inhibition of Collagen, Type IV, Alpha 3 (Goodpasture antigen) (COL4A3, Accession NM\_000091). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A3. Protocadherin Beta 16 (PCDHB16, Accession NM\_020957) is another VGAM1578 host target gene. PCDHB16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHB16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.



Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB16 BINDING SITE, designated SEQ ID:21946, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53888] Another function of VGAM1578 is therefore inhibition of Protocadherin Beta 16 (PCDHB16, Accession NM\_020957), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHB16. The function of PCDHB16 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM931. Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM\_003242) is another VGAM1578 host target gene. TGFB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB2 BINDING SITE, designated SEQ ID:9243, to the nucleotide

sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53889] Another function of VGAM1578 is therefore inhibition of Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM\_003242). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB2. Zinc Finger Protein 146 (ZNF146, Accession NM\_007145) is another VGAM1578 host target gene. ZNF146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF146 BINDING SITE, designated SEQ ID:13995, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53890] Another function of VGAM1578 is therefore inhibition of Zinc Finger Protein 146 (ZNF146, Accession NM\_007145), a gene which binds zinc ions, DNA, and heparin. Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with ZNF146. The function of ZNF146 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM192. Angiomotin (AMOT, Accession NM\_133265) is another VGAM1578 host target gene. AMOT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMOT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOT BINDING SITE, designated SEQ ID:28415, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53891] Another function of VGAM1578 is therefore inhibition of Angiomotin (AMOT, Accession NM\_133265). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOT. Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM\_018270) is another VGAM1578 host target gene. C20orf20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf20, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf20 BINDING SITE, designated SEQ ID:20246, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53892] Another function of VGAM1578 is therefore inhibition of Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM\_018270). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf20. Deiodinase, Iodothyronine, Type II (DIO2, Accession NM\_013989) is another VGAM1578 host target gene. DIO2 BINDING SITE1 and DIO2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DIO2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIO2 BINDING SITE1 and DIO2 BINDING SITE2, designated SEQ ID:15171 and SEQ ID:6460 respectively, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53893] Another function of VGAM1578 is therefore inhibition of Deiodinase, Iodothyronine, Type II (DIO2, Accession NM\_013989). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIO2. FLJ10120 (Accession NM\_018001) is another VGAM1578 host target gene. FLJ10120 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10120 BINDING SITE, designated SEQ ID:19730, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53894] Another function of VGAM1578 is therefore inhibition of FLJ10120 (Accession NM\_018001). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10120. FLJ11722 (Accession NM\_024970) is another VGAM1578 host target gene. FLJ11722 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11722, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11722 BINDING SITE, designated SEQ ID:24522, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53895] Another function of VGAM1578 is therefore inhibition of FLJ11722 (Accession NM\_024970). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11722. Interleukin Enhancer Binding Factor 3, 90kDa (ILF3, Accession NM\_004516) is another VGAM1578 host target gene. ILF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ILF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ILF3 BINDING SITE, designated SEQ ID:10846, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53896] Another function of VGAM1578 is therefore inhibition of Interleukin Enhancer Binding Factor 3, 90kDa (ILF3, Ac-

cession NM\_004516). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ILF3. KIAA1005 (Accession XM\_051197) is another VGAM1578 host target gene. KIAA1005 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1005, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1005 BINDING SITE, designated SEQ ID:35777, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53897] Another function of VGAM1578 is therefore inhibition of KIAA1005 (Accession XM\_051197). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1005. KIAA1924 (Accession XM\_057091) is another VGAM1578 host target gene. KIAA1924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1924 BINDING SITE, designated SEQ ID:36480, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53898] Another function of VGAM1578 is therefore inhibition of KIAA1924 (Accession XM\_057091). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1924. LOC150005 (Accession XM\_097795) is another VGAM1578 host target gene. LOC150005 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150005, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150005 BINDING SITE, designated SEQ ID:41123, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53899] Another function of VGAM1578 is therefore inhibition of LOC150005 (Accession XM\_097795). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150005. LOC255231 (Accession XM\_170908) is an-



other VGAM1578 host target gene. LOC255231 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255231 BINDING SITE, designated SEQ ID:45674, to the nucleotide sequence of VGAM1578 RNA, herein designated VGAM RNA, also designated SEQ ID:4289.

[53900] Another function of VGAM1578 is therefore inhibition of LOC255231 (Accession XM\_170908). Accordingly, utilities of VGAM1578 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255231. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1579 (VGAM1579) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53901] VGAM1579 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1579 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[53902] VGAM1579 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1579 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53903] VGAM1579 gene encodes a VGAM1579 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1579 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1579 precursor RNA is designated SEQ ID:1565, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1565 is located at position 8880 relative to the genome of Rhopalosiphum Padi Virus.

[53904] VGAM1579 precursor RNA folds onto itself, forming VGAM1579 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53905] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1579 folded precursor RNA into VGAM1579 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1579 RNA is designated SEQ ID:4290, and is provided hereinbelow with reference to the sequence listing part.

[53906] VGAM1579 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1579 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1579 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53907] VGAM1579 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1579 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1579 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1579 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1579 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53908] The complementary binding of VGAM1579 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1579 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1579 host target RNA into VGAM1579 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53909] It is appreciated that VGAM1579 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1579 host target genes. The mRNA of each one of this plurality of VGAM1579 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1579 RNA, herein designated VGAM RNA, and which when bound by VGAM1579 RNA causes inhibition of translation of respective one or more VGAM1579 host target proteins.

[53910] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1579 gene, herein designated VGAM GENE, on one or more VGAM1579 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53911] It is yet further appreciated that a function of VGAM1579 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1579 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGAM1579 correlate with, and may be deduced from, the identity of the host target genes which VGAM1579 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53912] Nucleotide sequences of the VGAM1579 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1579 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1579 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1579 are further described hereinbelow with reference to Table 1.

[53913] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1579 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1579 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53914] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1579 gene, herein designated VGAM is inhibition of expression of VGAM1579 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1579 correlate with, and may be deduced from, the identity of the target genes which VGAM1579 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53915] MFN1 (Accession NM\_017927) is a VGAM1579 host target gene. MFN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MFN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of MFN1 BINDING SITE, designated SEQ ID:19601, to the nucleotide sequence of VGAM1579 RNA, herein designated VGAM RNA, also designated SEQ ID:4290.

[53916] A function of VGAM1579 is therefore inhibition of MFN1 (Accession NM\_017927). Accordingly, utilities of VGAM1579 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MFN1. LOC148764 (Accession XM\_086307) is another VGAM1579 host target gene. LOC148764 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148764, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148764 BINDING SITE, designated SEQ ID:38588, to the nucleotide sequence of VGAM1579 RNA, herein designated VGAM RNA, also designated SEQ ID:4290.

[53917] Another function of VGAM1579 is therefore inhibition of LOC148764 (Accession XM\_086307). Accordingly, utilities of VGAM1579 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148764. Fig. 1 further provides a conceptual descrip-



tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1580 (VGAM1580) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53918] VGAM1580 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1580 was detected is described hereinabove with reference to Figs. 1–8.

[53919] VGAM1580 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhopalosiphum Padi Virus. VGAM1580 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53920] VGAM1580 gene encodes a VGAM1580 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1580 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1580 precursor RNA is designated SEQ ID:1566, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1566 is located at position 8018 relative to the genome of Rhopalosiphum Padi Virus.

[53921] VGAM1580 precursor RNA folds onto itself, forming VGAM1580 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53922] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1580 folded precursor RNA into VGAM1580 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM1580 RNA is designated SEQ ID:4291, and is provided hereinbelow with reference to the sequence listing part.

[53923] VGAM1580 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1580 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1580 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53924] VGAM1580 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1580 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1580 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1580 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1580 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[53925] The complementary binding of VGAM1580 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1580 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1580 host target RNA into VGAM1580 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53926] It is appreciated that VGAM1580 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1580 host target genes. The mRNA of each one of this plurality of VGAM1580 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1580 RNA, herein designated VGAM RNA, and which when bound by VGAM1580 RNA causes inhibition of translation of respective one or more

VGAM1580 host target proteins.

[53927] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1580 gene, herein designated VGAM GENE, on one or more VGAM1580 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53928] It is yet further appreciated that a function of VGAM1580 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1580 include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus.

Specific functions, and accordingly utilities, of VGAM1580 correlate with, and may be deduced from, the identity of the host target genes which VGAM1580 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53929] Nucleotide sequences of the VGAM1580 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1580 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1580 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1580 are further described hereinbelow with reference to Table 1.

[53930] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1580 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1580 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53931] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1580 gene, herein designated VGAM is inhibition of expression of VGAM1580 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1580 correlate with, and may be deduced from, the identity of the target genes which VGAM1580 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53932] Period Homolog 2 (Drosophila) (PER2, Accession NM\_022817) is a VGAM1580 host target gene. PER2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER2 BINDING SITE, designated SEQ ID:23088, to the nucleotide sequence of VGAM1580 RNA, herein designated VGAM RNA, also designated SEQ ID:4291.

[53933] A function of VGAM1580 is therefore inhibition of Period Homolog 2 (Drosophila) (PER2, Accession NM\_022817), a gene which Period homolog 2; putative circadian clock protein; has a PAS dimerization domain. Accordingly, utilities of VGAM1580 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER2. The function of PER2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM74.AKL3L (Accession NM\_016282) is another VGAM1580 host target gene. AKL3L BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AKL3L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKL3L BINDING SITE, designated SEQ ID:18410, to the nucleotide sequence of VGAM1580 RNA, herein designated VGAM RNA, also designated SEQ ID:4291.

[53934] Another function of VGAM1580 is therefore inhibition of AKL3L (Accession NM\_016282). Accordingly, utilities of VGAM1580 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKL3L. FLJ20793 (Accession XM\_166296) is another VGAM1580 host target gene. FLJ20793 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20793, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20793 BINDING SITE, designated SEQ ID:44110, to the nucleotide sequence of VGAM1580 RNA, herein designated VGAM RNA, also des-



ignated SEQ ID:4291.

[53935] Another function of VGAM1580 is therefore inhibition of FLJ20793 (Accession XM\_166296). Accordingly, utilities of VGAM1580 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20793. KIAA1715 (Accession XM\_042834) is another VGAM1580 host target gene. KIAA1715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1715 BINDING SITE, designated SEQ ID:33794, to the nucleotide sequence of VGAM1580 RNA, herein designated VGAM RNA, also designated SEQ ID:4291.

[53936] Another function of VGAM1580 is therefore inhibition of KIAA1715 (Accession XM\_042834). Accordingly, utilities of VGAM1580 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1715. Protein Tyrosine Phosphatase, Receptor Type, N Polypeptide 2 (PTPRN2, Accession NM\_130842) is another VGAM1580 host target gene. PTPRN2 BINDING SITE1 and PTPRN2 BINDING SITE2 are HOST TARGET binding

sites found in untranslated regions of mRNA encoded by PTPRN2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRN2 BINDING SITE1 and PTPRN2 BINDING SITE2, designated SEQ ID:28370 and SEQ ID:28375 respectively, to the nucleotide sequence of VGAM1580 RNA, herein designated VGAM RNA, also designated SEQ ID:4291.

[53937] Another function of VGAM1580 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, N Polypeptide 2 (PTPRN2, Accession NM\_130842). Accordingly, utilities of VGAM1580 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRN2. LOC203286 (Accession XM\_117526) is another VGAM1580 host target gene. LOC203286 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203286 BINDING SITE, designated SEQ ID:43498, to the nucleotide sequence of VGAM1580 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4291.

[53938] Another function of VGAM1580 is therefore inhibition of LOC203286 (Accession XM\_117526). Accordingly, utilities of VGAM1580 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203286. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1581 (VGAM1581) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53939] VGAM1581 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1581 was detected is described hereinabove with reference to Figs. 1–8.

[53940] VGAM1581 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1581 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53941] VGAM1581 gene encodes a VGAM1581 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1581 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1581 precursor RNA is designated SEQ ID:1567, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1567 is located at position 94704 relative to the genome of Saimiriine Herpesvirus 2.

[53942] VGAM1581 precursor RNA folds onto itself, forming VGAM1581 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53943] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1581 folded precursor RNA into VGAM1581 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM1581 RNA is designated SEQ ID:4292, and is provided hereinbelow with reference to the sequence listing part.

[53944] VGAM1581 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1581 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1581 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53945] VGAM1581 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1581 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1581 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1581 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1581 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53946] The complementary binding of VGAM1581 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1581 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1581 host target RNA into VGAM1581 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53947] It is appreciated that VGAM1581 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1581 host target genes. The mRNA of

each one of this plurality of VGAM1581 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1581 RNA, herein designated VGAM RNA, and which when bound by VGAM1581 RNA causes inhibition of translation of respective one or more VGAM1581 host target proteins.

[53948] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1581 gene, herein designated VGAM GENE, on one or more VGAM1581 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[53949] It is yet further appreciated that a function of VGAM1581 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1581 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1581 correlate with, and may be deduced from, the identity of the host target genes which VGAM1581 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53950] Nucleotide sequences of the VGAM1581 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1581 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1581 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1581 are further described hereinbelow with reference to Table 1.

[53951] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1581 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1581 RNA,



herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53952] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1581 gene, herein designated VGAM is inhibition of expression of VGAM1581 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1581 correlate with, and may be deduced from, the identity of the target genes which VGAM1581 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53953] Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM\_042963) is a VGAM1581 host target gene. ARHGEF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF6 BINDING SITE, designated SEQ ID:33845, to the nucleotide sequence of VGAM1581 RNA, herein designated VGAM RNA, also designated SEQ ID:4292.

[53954] A function of VGAM1581 is therefore inhibition of Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6

(ARHGEF6, Accession XM\_042963). Accordingly, utilities of VGAM1581 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF6. D4ST-1 (Accession NM\_130468) is another VGAM1581 host target gene. D4ST-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by D4ST-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D4ST-1 BINDING SITE, designated SEQ ID:28228, to the nucleotide sequence of VGAM1581 RNA, herein designated VGAM RNA, also designated SEQ ID:4292.

[53955] Another function of VGAM1581 is therefore inhibition of D4ST-1 (Accession NM\_130468). Accordingly, utilities of VGAM1581 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D4ST-1. KIAA0700 (Accession XM\_050561) is another VGAM1581 host target gene. KIAA0700 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0700 BINDING SITE, designated SEQ ID:35658, to the nucleotide sequence of VGAM1581 RNA, herein designated VGAM RNA, also designated SEQ ID:4292.

[53956] Another function of VGAM1581 is therefore inhibition of KIAA0700 (Accession XM\_050561). Accordingly, utilities of VGAM1581 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0700. RODH-4 (Accession NM\_003708) is another VGAM1581 host target gene. RODH-4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RODH-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RODH-4 BINDING SITE, designated SEQ ID:9808, to the nucleotide sequence of VGAM1581 RNA, herein designated VGAM RNA, also designated SEQ ID:4292.

[53957] Another function of VGAM1581 is therefore inhibition of RODH-4 (Accession NM\_003708). Accordingly, utilities of VGAM1581 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RODH-4. Serine Palmitoyltransferase, Long Chain Base Subunit 2

(SPTLC2, Accession NM\_004863) is another VGAM1581 host target gene. SPTLC2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SPTLC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTLC2 BINDING SITE, designated SEQ ID:11283, to the nucleotide sequence of VGAM1581 RNA, herein designated VGAM RNA, also designated SEQ ID:4292.

[53958] Another function of VGAM1581 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM\_004863). Accordingly, utilities of VGAM1581 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. LOC147669 (Accession XM\_097262) is another VGAM1581 host target gene. LOC147669 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC147669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147669 BINDING SITE, designated SEQ ID:40856, to

the nucleotide sequence of VGAM1581 RNA, herein designated VGAM RNA, also designated SEQ ID:4292.

[53959] Another function of VGAM1581 is therefore inhibition of LOC147669 (Accession XM\_097262). Accordingly, utilities of VGAM1581 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147669. LOC151438 (Accession XM\_098060) is another VGAM1581 host target gene. LOC151438 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151438 BINDING SITE, designated SEQ ID:41347, to the nucleotide sequence of VGAM1581 RNA, herein designated VGAM RNA, also designated SEQ ID:4292.

[53960] Another function of VGAM1581 is therefore inhibition of LOC151438 (Accession XM\_098060). Accordingly, utilities of VGAM1581 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151438. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1582 (VGAM1582) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53961] VGAM1582 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1582 was detected is described hereinabove with reference to Figs. 1–8.

[53962] VGAM1582 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1582 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53963] VGAM1582 gene encodes a VGAM1582 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1582 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1582 precursor RNA is designated SEQ ID:1568, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1568 is located at position 90201 relative to the genome of Saimiriine Herpesvirus 2.

[53964] VGAM1582 precursor RNA folds onto itself, forming VGAM1582 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53965] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1582 folded precursor RNA into VGAM1582 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1582 RNA is designated SEQ ID:4293, and is provided hereinbelow with reference to the sequence listing part.

[53966] VGAM1582 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1582 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1582 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[53967] VGAM1582 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1582 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1582 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1582 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1582 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding



sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[53968] The complementary binding of VGAM1582 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1582 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1582 host target RNA into VGAM1582 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53969] It is appreciated that VGAM1582 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1582 host target genes. The mRNA of each one of this plurality of VGAM1582 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1582 RNA, herein designated VGAM RNA, and which when bound by VGAM1582 RNA causes inhibition of translation of respective one or more VGAM1582 host target proteins.

[53970] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1582 gene, herein designated VGAM GENE, on one or more VGAM1582 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[53971] It is yet further appreciated that a function of VGAM1582 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1582 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1582 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[53972] Nucleotide sequences of the VGAM1582 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1582 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1582 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1582 are further described hereinbelow with reference to Table 1.

[53973] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1582 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1582 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[53974] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1582 gene, herein designated VGAM is inhibition of expression of VGAM1582 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1582 correlate with, and may be deduced from, the identity of the target genes which VGAM1582

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[53975] Cyclin-dependent Kinase Inhibitor 2A (melanoma, p16, inhibits CDK4) (CDKN2A, Accession NM\_058197) is a VGAM1582 host target gene. CDKN2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDKN2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN2A BINDING SITE, designated SEQ ID:27759, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53976] A function of VGAM1582 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 2A (melanoma, p16, inhibits CDK4) (CDKN2A, Accession NM\_058197). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN2A. Secreted Frizzled-related Protein 1 (SFRP1, Accession NM\_003012) is another VGAM1582 host target gene. SFRP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRP1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRP1 BINDING SITE, designated SEQ ID:8924, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53977] Another function of VGAM1582 is therefore inhibition of Secreted Frizzled-related Protein 1 (SFRP1, Accession NM\_003012), a gene which is a receptor for wnt proteins that may have an anti-apoptotic function. Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRP1. The function of SFRP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM250. APACD (Accession NM\_005783) is another VGAM1582 host target gene. APACD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APACD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APACD BINDING SITE, designated SEQ ID:12362, to the

nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53978] Another function of VGAM1582 is therefore inhibition of APACD (Accession NM\_005783). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APACD. ARNTL2 (Accession NM\_020183) is another VGAM1582 host target gene. ARNTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARNTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNTL2 BINDING SITE, designated SEQ ID:21409, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53979] Another function of VGAM1582 is therefore inhibition of ARNTL2 (Accession NM\_020183). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNTL2. DIS3 (Accession NM\_014953) is another VGAM1582 host target gene. DIS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by DIS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIS3 BINDING SITE, designated SEQ ID:17304, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53980] Another function of VGAM1582 is therefore inhibition of DIS3 (Accession NM\_014953). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIS3. DKFZP564B1162 (Accession NM\_031305) is another VGAM1582 host target gene. DKFZP564B1162 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP564B1162, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564B1162 BINDING SITE, designated SEQ ID:25339, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53981] Another function of VGAM1582 is therefore inhibition of

DKFZP564B1162 (Accession NM\_031305). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564B1162. GT650 (Accession NM\_052851) is another VGAM1582 host target gene. GT650 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GT650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GT650 BINDING SITE, designated SEQ ID:27433, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53982] Another function of VGAM1582 is therefore inhibition of GT650 (Accession NM\_052851). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GT650. HTEX4 (Accession XM\_166378) is another VGAM1582 host target gene. HTEX4 BINDING SITE1 through HTEX4 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HTEX4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-



trates the complementarity of the nucleotide sequences of HTEX4 BINDING SITE1 through HTEX4 BINDING SITE3, designated SEQ ID:44218, SEQ ID:46654 and SEQ ID:46723 respectively, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53983] Another function of VGAM1582 is therefore inhibition of HTEX4 (Accession XM\_166378). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTEX4. KIAA0830 (Accession XM\_045759) is another VGAM1582 host target gene. KIAA0830 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0830, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0830 BINDING SITE, designated SEQ ID:34544, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53984] Another function of VGAM1582 is therefore inhibition of KIAA0830 (Accession XM\_045759). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0830. KIAA1254 (Accession XM\_046132) is another VGAM1582 host target gene. KIAA1254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1254 BINDING SITE, designated SEQ ID:34697, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53985] Another function of VGAM1582 is therefore inhibition of KIAA1254 (Accession XM\_046132). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1254. MGC2827 (Accession NM\_023940) is another VGAM1582 host target gene. MGC2827 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2827 BINDING SITE, designated SEQ ID:23427, to the nucleotide

sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53986] Another function of VGAM1582 is therefore inhibition of MGC2827 (Accession NM\_023940). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2827. LOC158798 (Accession XM\_088671) is another VGAM1582 host target gene. LOC158798 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158798 BINDING SITE, designated SEQ ID:39891, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53987] Another function of VGAM1582 is therefore inhibition of LOC158798 (Accession XM\_088671). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158798. LOC161357 (Accession XM\_090827) is another VGAM1582 host target gene. LOC161357 BINDING SITE is HOST TARGET binding site found in the 3` un-

translated region of mRNA encoded by LOC161357, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161357 BINDING SITE, designated SEQ ID:40017, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53988] Another function of VGAM1582 is therefore inhibition of LOC161357 (Accession XM\_090827). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161357. LOC199863 (Accession XM\_117147) is another VGAM1582 host target gene. LOC199863 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199863, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199863 BINDING SITE, designated SEQ ID:43253, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53989] Another function of VGAM1582 is therefore inhibition of LOC199863 (Accession XM\_117147). Accordingly, utilities

of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199863. LOC221895 (Accession XM\_166511) is another VGAM1582 host target gene. LOC221895 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221895 BINDING SITE, designated SEQ ID:44440, to the nucleotide sequence of VGAM1582 RNA, herein designated VGAM RNA, also designated SEQ ID:4293.

[53990] Another function of VGAM1582 is therefore inhibition of LOC221895 (Accession XM\_166511). Accordingly, utilities of VGAM1582 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221895. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1583 (VGAM1583) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[53991] VGAM1583 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1583 was detected is described hereinabove with reference to Figs. 1–8.

[53992] VGAM1583 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1583 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[53993] VGAM1583 gene encodes a VGAM1583 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1583 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1583 precursor RNA is designated SEQ ID:1569, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1569 is located at position 93157 relative to the genome of Saimiriine Herpesvirus 2.

[53994] VGAM1583 precursor RNA folds onto itself, forming VGAM1583 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[53995] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1583 folded precursor RNA into VGAM1583 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 63%) nucleotide sequence of VGAM1583 RNA is designated SEQ ID:4294, and is provided hereinbelow with reference to the sequence listing part.

[53996] VGAM1583 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1583 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1583 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[53997] VGAM1583 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1583 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1583 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1583 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1583 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.



[53998] The complementary binding of VGAM1583 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1583 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1583 host target RNA into VGAM1583 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[53999] It is appreciated that VGAM1583 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1583 host target genes. The mRNA of each one of this plurality of VGAM1583 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1583 RNA, herein designated VGAM RNA, and which when bound by VGAM1583 RNA causes inhibition of translation of respective one or more VGAM1583 host target proteins.

[54000] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1583 gene, herein designated VGAM GENE, on one or more VGAM1583 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54001] It is yet further appreciated that a function of VGAM1583 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1583 correlate with, and may be deduced from, the identity of the host target genes which VGAM1583 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54002] Nucleotide sequences of the VGAM1583 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1583 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1583 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1583 are further  
described hereinbelow with reference to Table 1.

[54003] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1583 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1583 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[54004] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1583 gene, herein designated VGAM is  
inhibition of expression of VGAM1583 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1583 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1583  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[54005] Fibronectin Leucine Rich Transmembrane Protein 2  
(FLRT2, Accession NM\_013231) is a VGAM1583 host tar-

get gene. FLRT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14874, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54006] A function of VGAM1583 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM\_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 duncce homolog, *Drosophila*) (PDE4D, Accession XM\_056815) is another VGAM1583 host target gene. PDE4D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by PDE4D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4D BINDING SITE, designated SEQ ID:36427, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54007] Another function of VGAM1583 is therefore inhibition of Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, *Drosophila*) (PDE4D, Accession XM\_056815), a gene which has similarity to *Drosophila* dnc, which is the affected protein in learning and memory mutant dunce. Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4D. The function of PDE4D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Toll-like 1 (TLL1, Accession NM\_012464) is another VGAM1583 host target gene. TLL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TLL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLL1 BINDING SITE, designated SEQ ID:14836, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54008] Another function of VGAM1583 is therefore inhibition of Tolloid-like 1 (TLL1, Accession NM\_012464), a gene which is involved in bone morphogenesis. Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLL1. The function of TLL1 has been established by previous studies. Scott et al. (1999) compared enzymatic activities and expression domains of 4 mammalian BMP1/TLD-like proteases and found differences in their ability to process fibrillar collagen precursors and to cleave chordin (OMIM Ref. No. 603475). As previously demonstrated for BMP1 and TLD, TLL1 specifically processes procollagen C-propeptides at the physiologically relevant site, whereas TLL2 (OMIM Ref. No. 606743) lacks this activity. BMP1 and TLL1 cleave chordin, at sites similar to procollagen C-propeptide cleavage sites, and counteract dorsalizing effects of chordin upon overexpression on *Xenopus* embryos. Proteases TLD and TLL2 do not

cleave chordin. Animal model experiments lend further support to the function of TLL1. Clark et al. (1999) used gene targeting in embryonic stem cells to produce mice with a disrupted allele for Tll1. Homozygous mutants were embryonic lethal, with death at midgestation from cardiac failure and a constellation of developmental defects confined to the heart. Constant features were incomplete formation of the muscular interventricular septum and an abnormal and novel positioning of the heart and aorta.

[54009] It is appreciated that the abovementioned animal model for TLL1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[54010] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54011] Scott, I. C.; Blitz, I. L.; Pappano, W. N.; Imamura, Y.; Clark, T. G.; Steiglitz, B. M.; Thomas, C. L.; Maas, S. A.; Takahara, K.; Cho, K. W. Y.; Greenspan, D. S. : Mammalian BMP-1/tolloid-related metalloproteinases, including novel family member mammalian tolloid-like 2, have differential enzymatic activities and distributions of expression relevant to patterning and skeletogenesis. Dev. Biol. 213:

283–300, 1999. ; and

[54012] Clark, T. G.; Conway, S. J.; Scott, I. C.; Labosky, P. A.; Win-  
nier, G.; Bundy, J.; Hogan, B. L. M.; Greenspan, D. S. : The  
mammalian Tolloid-like 1 gene, Tll1, is necessary for nor-  
mal s.

[54013] Further studies establishing the function and utilities of  
TLL1 are found in John Hopkins OMIM database record ID  
606742, and in cited publications numbered 548 and  
5483–5484 listed in the bibliography section hereinbelow,  
which are also hereby incorporated by refer-  
ence. Aldo-keto Reductase Family 1, Member D1 (delta  
4–3–ketosteroid–5–beta–reductase) (AKR1D1, Accession  
NM\_005989) is another VGAM1583 host target gene.  
AKR1D1 BINDING SITE is HOST TARGET binding site found  
in the 3` untranslated region of mRNA encoded by  
AKR1D1, corresponding to a HOST TARGET binding site  
such as BINDING SITE I, BINDING SITE II or BINDING SITE III.  
Table 2 illustrates the complementarity of the nucleotide  
sequences of AKR1D1 BINDING SITE, designated SEQ  
ID:12609, to the nucleotide sequence of VGAM1583 RNA,  
herein designated VGAM RNA, also designated SEQ  
ID:4294.

[54014] Another function of VGAM1583 is therefore inhibition of



Aldo-keto Reductase Family 1, Member D1 (delta 4-3-ketosteroid-5-beta-reductase) (AKR1D1, Accession NM\_005989). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKR1D1. FLJ14803 (Accession NM\_032842) is another VGAM1583 host target gene. FLJ14803 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14803, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14803 BINDING SITE, designated SEQ ID:26625, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54015] Another function of VGAM1583 is therefore inhibition of FLJ14803 (Accession NM\_032842). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14803. FLJ22795 (Accession NM\_025084) is another VGAM1583 host target gene. FLJ22795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22795, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22795 BINDING SITE, designated SEQ ID:24686, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54016] Another function of VGAM1583 is therefore inhibition of FLJ22795 (Accession NM\_025084). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22795. H2A Histone Family, Member J (H2AFJ, Accession NM\_018267) is another VGAM1583 host target gene. H2AFJ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H2AFJ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H2AFJ BINDING SITE, designated SEQ ID:20235, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54017] Another function of VGAM1583 is therefore inhibition of H2A Histone Family, Member J (H2AFJ, Accession

NM\_018267). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H2AFJ. KIAA0737 (Accession NM\_014828) is another VGAM1583 host target gene. KIAA0737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0737 BINDING SITE, designated SEQ ID:16818, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54018] Another function of VGAM1583 is therefore inhibition of KIAA0737 (Accession NM\_014828). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0737. KIAA1582 (Accession XM\_037262) is another VGAM1583 host target gene. KIAA1582 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1582, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1582 BINDING SITE, designated SEQ ID:32577, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54019] Another function of VGAM1583 is therefore inhibition of KIAA1582 (Accession XM\_037262). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1582. PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM\_028335) is another VGAM1583 host target gene. PRPF8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRPF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPF8 BINDING SITE, designated SEQ ID:30683, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54020] Another function of VGAM1583 is therefore inhibition of PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM\_028335). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PRPF8. Syntrophin, Gamma 1 (SNTG1, Accession NM\_018967) is another VGAM1583 host target gene. SNTG1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNTG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNTG1 BINDING SITE, designated SEQ ID:21040, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54021] Another function of VGAM1583 is therefore inhibition of Syntrophin, Gamma 1 (SNTG1, Accession NM\_018967). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNTG1. LOC143465 (Accession XM\_096430) is another VGAM1583 host target gene. LOC143465 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC143465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143465 BINDING SITE, desig-

nated SEQ ID:40363, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54022] Another function of VGAM1583 is therefore inhibition of LOC143465 (Accession XM\_096430). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143465. LOC145717 (Accession XM\_039771) is another VGAM1583 host target gene. LOC145717 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145717, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145717 BINDING SITE, designated SEQ ID:33186, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54023] Another function of VGAM1583 is therefore inhibition of LOC145717 (Accession XM\_039771). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145717. LOC145725 (Accession XM\_085211) is another VGAM1583 host target gene. LOC145725 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145725 BINDING SITE, designated SEQ ID:37943, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54024] Another function of VGAM1583 is therefore inhibition of LOC145725 (Accession XM\_085211). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145725. LOC145732 (Accession XM\_085218) is another VGAM1583 host target gene. LOC145732 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145732, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145732 BINDING SITE, designated SEQ ID:37952, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54025] Another function of VGAM1583 is therefore inhibition of LOC145732 (Accession XM\_085218). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145732. LOC196957 (Accession XM\_113789) is another VGAM1583 host target gene. LOC196957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196957 BINDING SITE, designated SEQ ID:42424, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54026] Another function of VGAM1583 is therefore inhibition of LOC196957 (Accession XM\_113789). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC196957. LOC196961 (Accession XM\_113790) is another VGAM1583 host target gene. LOC196961 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196961 BINDING SITE, designated SEQ ID:42433, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54027] Another function of VGAM1583 is therefore inhibition of LOC196961 (Accession XM\_113790). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196961. LOC197138 (Accession XM\_113829) is another VGAM1583 host target gene. LOC197138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197138 BINDING SITE, designated SEQ ID:42451, to the nucleotide sequence of VGAM1583 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4294.

[54028] Another function of VGAM1583 is therefore inhibition of LOC197138 (Accession XM\_113829). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197138. LOC201475 (Accession XM\_113967) is another VGAM1583 host target gene. LOC201475 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201475 BINDING SITE, designated SEQ ID:42577, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54029] Another function of VGAM1583 is therefore inhibition of LOC201475 (Accession XM\_113967). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201475. LOC220537 (Accession XM\_165406) is another VGAM1583 host target gene. LOC220537 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220537, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220537 BINDING SITE, designated SEQ ID:43619, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54030] Another function of VGAM1583 is therefore inhibition of LOC220537 (Accession XM\_165406). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220537. LOC221806 (Accession XM\_166518) is another VGAM1583 host target gene. LOC221806 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221806, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221806 BINDING SITE, designated SEQ ID:44452, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54031] Another function of VGAM1583 is therefore inhibition of LOC221806 (Accession XM\_166518). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC221806. LOC245727 (Accession XM\_165913) is another VGAM1583 host target gene. LOC245727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC245727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245727 BINDING SITE, designated SEQ ID:43793, to the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54032] Another function of VGAM1583 is therefore inhibition of LOC245727 (Accession XM\_165913). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245727. LOC254065 (Accession XM\_173239) is another VGAM1583 host target gene. LOC254065 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254065, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254065 BINDING SITE, designated SEQ ID:46524, to

the nucleotide sequence of VGAM1583 RNA, herein designated VGAM RNA, also designated SEQ ID:4294.

[54033] Another function of VGAM1583 is therefore inhibition of LOC254065 (Accession XM\_173239). Accordingly, utilities of VGAM1583 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254065. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1584 (VGAM1584) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54034] VGAM1584 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1584 was detected is described hereinabove with reference to Figs. 1–8.

[54035] VGAM1584 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1584 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54036] VGAM1584 gene encodes a VGAM1584 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1584 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1584 precursor RNA is designated SEQ ID:1570, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1570 is located at position 91273 relative to the genome of Saimiriine Herpesvirus 2.

[54037] VGAM1584 precursor RNA folds onto itself, forming VGAM1584 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54038] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1584 folded precursor RNA into VGAM1584 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1584 RNA is designated SEQ ID:4295, and is provided hereinbelow with reference to the sequence listing part.

[54039] VGAM1584 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1584 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1584 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54040] VGAM1584 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1584 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1584 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1584 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1584 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54041] The complementary binding of VGAM1584 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1584 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1584 host target RNA into VGAM1584 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54042] It is appreciated that VGAM1584 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM1584 host target genes. The mRNA of each one of this plurality of VGAM1584 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1584 RNA, herein designated VGAM RNA, and which when bound by VGAM1584 RNA causes inhibition of translation of respective one or more VGAM1584 host target proteins.

[54043] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1584 gene, herein designated VGAM GENE, on one or more VGAM1584 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[54044] It is yet further appreciated that a function of VGAM1584 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1584 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1584 correlate with, and may be deduced from, the identity of the host target genes which VGAM1584 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54045] Nucleotide sequences of the VGAM1584 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1584 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1584 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1584 are further described hereinbelow with reference to Table 1.

[54046] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1584 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1584 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54047] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1584 gene, herein designated VGAM is inhibition of expression of VGAM1584 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1584 correlate with, and may be deduced from, the identity of the target genes which VGAM1584 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54048] FLJ20456 (Accession NM\_017831) is a VGAM1584 host target gene. FLJ20456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20456 BINDING SITE, designated SEQ ID:19493, to the nucleotide sequence of VGAM1584 RNA, herein designated VGAM RNA, also designated SEQ ID:4295.

[54049] A function of VGAM1584 is therefore inhibition of FLJ20456 (Accession NM\_017831). Accordingly, utilities of

VGAM1584 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20456. KIAA1582 (Accession XM\_037262) is another VGAM1584 host target gene. KIAA1582 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1582, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1582 BINDING SITE, designated SEQ ID:32578, to the nucleotide sequence of VGAM1584 RNA, herein designated VGAM RNA, also designated SEQ ID:4295.

[54050] Another function of VGAM1584 is therefore inhibition of KIAA1582 (Accession XM\_037262). Accordingly, utilities of VGAM1584 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1582. Tripartite Motif-containing 38 (TRIM38, Accession NM\_006355) is another VGAM1584 host target gene. TRIM38 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM38, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of TRIM38 BINDING SITE, designated SEQ ID:13049, to the nucleotide sequence of VGAM1584 RNA, herein designated VGAM RNA, also designated SEQ ID:4295.

[54051] Another function of VGAM1584 is therefore inhibition of Tripartite Motif-containing 38 (TRIM38, Accession NM\_006355). Accordingly, utilities of VGAM1584 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM38. LOC219673 (Accession XM\_167567) is another VGAM1584 host target gene. LOC219673 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219673, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219673 BINDING SITE, designated SEQ ID:44691, to the nucleotide sequence of VGAM1584 RNA, herein designated VGAM RNA, also designated SEQ ID:4295.

[54052] Another function of VGAM1584 is therefore inhibition of LOC219673 (Accession XM\_167567). Accordingly, utilities of VGAM1584 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC219673. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1585 (VGAM1585) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54053] VGAM1585 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1585 was detected is described hereinabove with reference to Figs. 1–8.

[54054] VGAM1585 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1585 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54055] VGAM1585 gene encodes a VGAM1585 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1585 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1585 precursor RNA is designated SEQ ID:1571, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1571 is located at position 87716 relative to the genome of Saimiriine Herpesvirus 2.

- [54056] VGAM1585 precursor RNA folds onto itself, forming VGAM1585 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54057] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1585 folded precursor RNA into VGAM1585 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1585 RNA is designated SEQ ID:4296, and is provided hereinbelow with reference to the sequence listing part.

[54058] VGAM1585 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1585 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1585 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[54059] VGAM1585 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1585 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1585 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1585 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in



untranslated regions of a VGAM1585 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54060] The complementary binding of VGAM1585 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1585 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1585 host target RNA into VGAM1585 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54061] It is appreciated that VGAM1585 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1585 host target genes. The mRNA of each one of this plurality of VGAM1585 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1585 RNA, herein designated VGAM RNA, and which when bound by VGAM1585 RNA causes

inhibition of translation of respective one or more VGAM1585 host target proteins.

[54062] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1585 gene, herein designated VGAM GENE, on one or more VGAM1585 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54063] It is yet further appreciated that a function of VGAM1585 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1585 include diagnosis, prevention and

treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1585 correlate with, and may be deduced from, the identity of the host target genes which VGAM1585 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54064] Nucleotide sequences of the VGAM1585 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1585 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1585 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1585 are further described hereinbelow with reference to Table 1.

[54065] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1585 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1585 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54066] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1585 gene, herein designated VGAM is inhibition of expression of VGAM1585 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1585 correlate with, and may be deduced from, the identity of the target genes which VGAM1585 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54067] Chloride Channel, Calcium Activated, Family Member 3 (CLCA3, Accession NM\_004921) is a VGAM1585 host target gene. CLCA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLCA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCA3 BINDING SITE, designated SEQ ID:11353, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.

[54068] A function of VGAM1585 is therefore inhibition of Chloride Channel, Calcium Activated, Family Member 3 (CLCA3, Accession NM\_004921), a gene which is similar to calcium-activated chloride channel family. Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCA3. The function of CLCA3 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM595. Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM\_005228) is another VGAM1585 host target gene. EGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFR BINDING SITE, designated SEQ ID:11719, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.

[54069] Another function of VGAM1585 is therefore inhibition of Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM\_005228), a gene which is a receptor for egf, but also for other members of the egf family. Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFR. The function of EGFR and its association with various diseases and clinical conditions, has

been established by previous studies, as described hereinabove with reference to VGAM229. G Protein-coupled Receptor 48 (GPR48, Accession NM\_018490) is another VGAM1585 host target gene. GPR48 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR48, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR48 BINDING SITE, designated SEQ ID:20552, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.

[54070] Another function of VGAM1585 is therefore inhibition of G Protein-coupled Receptor 48 (GPR48, Accession NM\_018490), a gene which binds to follicle-stimulating hormone and thyroid-stimulating hormone. Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR48. The function of GPR48 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM376. Pleiomorphic Adenoma Gene 1 (PLAG1, Accession NM\_002655) is another VGAM1585

host target gene. PLAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAG1 BINDING SITE, designated SEQ ID:8525, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.

[54071] Another function of VGAM1585 is therefore inhibition of Pleiomorphic Adenoma Gene 1 (PLAG1, Accession NM\_002655), a gene which contains a zinc finger domain. Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAG1. The function of PLAG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM29. Deiodinase, Iodothyronine, Type II (DIO2, Accession NM\_000793) is another VGAM1585 host target gene. DIO2 BINDING SITE1 and DIO2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DIO2, corresponding to HOST TARGET

binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIO2 BINDING SITE1 and DIO2 BINDING SITE2, designated SEQ ID:6459 and SEQ ID:15170 respectively, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.

[54072] Another function of VGAM1585 is therefore inhibition of Deiodinase, Iodothyronine, Type II (DIO2, Accession NM\_000793). Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIO2. Solute Carrier Family 7, (cationic amino acid transporter,  $\gamma^+$  system) Member 11 (SLC7A11, Accession NM\_014331) is another VGAM1585 host target gene. SLC7A11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A11 BINDING SITE, designated SEQ ID:15646, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.



[54073] Another function of VGAM1585 is therefore inhibition of Solute Carrier Family 7, (cationic amino acid transporter, y<sup>+</sup> system) Member 11 (SLC7A11, Accession NM\_014331). Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A11. SRY (sex determining region Y)-box 7 (SOX7, Accession NM\_031439) is another VGAM1585 host target gene. SOX7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOX7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX7 BINDING SITE, designated SEQ ID:25450, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.

[54074] Another function of VGAM1585 is therefore inhibition of SRY (sex determining region Y)-box 7 (SOX7, Accession NM\_031439). Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOX7. LOC158629 (Accession XM\_098972) is another VGAM1585 host target gene. LOC158629 BINDING SITE is HOST TARGET binding

site found in the 5` untranslated region of mRNA encoded by LOC158629, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158629 BINDING SITE, designated SEQ ID:42017, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.

[54075] Another function of VGAM1585 is therefore inhibition of LOC158629 (Accession XM\_098972). Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158629. LOC168512 (Accession XM\_095148) is another VGAM1585 host target gene. LOC168512 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC168512, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168512 BINDING SITE, designated SEQ ID:40252, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.

[54076] Another function of VGAM1585 is therefore inhibition of

LOC168512 (Accession XM\_095148). Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168512. LOC51205 (Accession NM\_016361) is another VGAM1585 host target gene. LOC51205 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51205 BINDING SITE, designated SEQ ID:18501, to the nucleotide sequence of VGAM1585 RNA, herein designated VGAM RNA, also designated SEQ ID:4296.

[54077] Another function of VGAM1585 is therefore inhibition of LOC51205 (Accession NM\_016361). Accordingly, utilities of VGAM1585 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51205. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1586 (VGAM1586) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[54078] VGAM1586 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1586 was detected is described hereinabove with reference to Figs. 1–8.

[54079] VGAM1586 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1586 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54080] VGAM1586 gene encodes a VGAM1586 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1586 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1586 precursor RNA is designated SEQ ID:1572, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1572 is located at position 86610 relative to the genome of Saimiriine Herpesvirus 2.

[54081] VGAM1586 precursor RNA folds onto itself, forming VGAM1586 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54082] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1586 folded precursor RNA into VGAM1586 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 74%) nucleotide sequence of VGAM1586 RNA is designated SEQ ID:4297, and is provided hereinbelow with reference to the sequence listing part.

[54083] VGAM1586 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1586 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1586 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[54084] VGAM1586 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1586 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1586 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1586 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1586 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[54085] The complementary binding of VGAM1586 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1586 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1586 host target RNA into VGAM1586 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54086] It is appreciated that VGAM1586 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1586 host target genes. The mRNA of each one of this plurality of VGAM1586 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1586 RNA, herein designated VGAM RNA, and which when bound by VGAM1586 RNA causes inhibition of translation of respective one or more VGAM1586 host target proteins.

[54087] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1586 gene, herein designated VGAM GENE, on one

or more VGAM1586 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54088] It is yet further appreciated that a function of VGAM1586 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1586 correlate with, and may be deduced from, the identity of the host target genes which VGAM1586 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[54089] Nucleotide sequences of the VGAM1586 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1586 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1586 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1586 are further described hereinbelow with reference to Table 1.

[54090] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1586 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1586 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54091] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1586 gene, herein designated VGAM is inhibition of expression of VGAM1586 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1586 correlate with, and may be deduced from, the identity of the target genes which VGAM1586 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54092] Guanine Nucleotide Binding Protein (G protein), Gamma

Transducing Activity Polypeptide 2 (GNGT2, Accession NM\_031498) is a VGAM1586 host target gene. GNGT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GNGT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNGT2 BINDING SITE, designated SEQ ID:25578, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54093] A function of VGAM1586 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Gamma Transducing Activity Polypeptide 2 (GNGT2, Accession NM\_031498), a gene which is involved as a modulator or transducer in various transmembrane signaling systems. Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNGT2. The function of GNGT2 has been established by previous studies. Phototransduction in the vertebrate rod and cone photoreceptors is regulated by structurally homologous but distinct groups of signaling proteins. Ong et al. (1995) identified in bovine retinas a cone-specific G protein gamma subunit, G-gamma-c

(previously named G-gamma-8), which may play a key role in coupling the cone visual pigment to phosphodiesterase. Ong et al. (1997) characterized the human homolog, which was found to share a high degree of sequence identity with the corresponding bovine isoform (85%) and human rod G-gamma-1 (63%). The protein is specifically localized in cones, as indicated by immunohistochemical staining. Nucleotide sequence analysis of the gene, designated GNGT2, showed a structure consisting of 3 exons and 2 introns, with the intron splice sites similar to those of the rod G-gamma-1 gene (GNGT1; 189970). By FISH, Ong et al. (1997) localized the GNGT2 gene to 17q21.

[54094] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54095] Ong, O. C.; Hu, K.; Rong, H.; Lee, R. H.; Fung, B. K.-K. : Gene structure and chromosome localization of the G-gamma-c subunit of human cone G-protein (GNGT2). Genomics 44: 101-109, 1997. ; and

[54096] Ong, O. C.; Yamane, H. K.; Phan, K. B.; Fong, H. K.; Bok, D.; Lee, R. H.; Fung, B. K.-K. : Molecular cloning and characterization of the G protein gamma subunit of cone pho-

toreceptors.

[54097] Further studies establishing the function and utilities of GNGT2 are found in John Hopkins OMIM database record ID 603655, and in cited publications numbered 5859–5860 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Golgi Complex Associated Protein 1, 60kDa (GOCAP1, Accession NM\_022735) is another VGAM1586 host target gene. GOCAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOCAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOCAP1 BINDING SITE, designated SEQ ID:22937, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54098] Another function of VGAM1586 is therefore inhibition of Golgi Complex Associated Protein 1, 60kDa (GOCAP1, Accession NM\_022735). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOCAP1. LIM Domains Containing 1 (LIMD1, Accession NM\_014240) is an–

other VGAM1586 host target gene. LIMD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMD1 BINDING SITE, designated SEQ ID:15498, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54099] Another function of VGAM1586 is therefore inhibition of LIM Domains Containing 1 (LIMD1, Accession NM\_014240). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMD1. Neuregulin 1 (NRG1, Accession NM\_013959) is another VGAM1586 host target gene. NRG1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NRG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRG1 BINDING SITE, designated SEQ ID:15139, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54100] Another function of VGAM1586 is therefore inhibition of Neuregulin 1 (NRG1, Accession NM\_013959), a gene which is essential for neuronal development. Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRG1. The function of NRG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1259. ADMP (Accession NM\_145035) is another VGAM1586 host target gene. ADMP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADMP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADMP BINDING SITE, designated SEQ ID:29653, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54101] Another function of VGAM1586 is therefore inhibition of ADMP (Accession NM\_145035). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADMP. BM045 (Accession XM\_085509) is another VGAM1586

host target gene. BM045 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BM045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BM045 BINDING SITE, designated SEQ ID:38214, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54102] Another function of VGAM1586 is therefore inhibition of BM045 (Accession XM\_085509). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BM045. Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM\_052966) is another VGAM1586 host target gene. C1orf24 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1orf24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf24 BINDING SITE, designated SEQ ID:27526, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ

ID:4297.

[54103] Another function of VGAM1586 is therefore inhibition of Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM\_052966). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf24. FLJ20093 (Accession NM\_017664) is another VGAM1586 host target gene. FLJ20093 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20093 BINDING SITE, designated SEQ ID:19204, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54104] Another function of VGAM1586 is therefore inhibition of FLJ20093 (Accession NM\_017664). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20093. FLJ22037 (Accession XM\_168215) is another VGAM1586 host target gene. FLJ22037 BINDING SITE is HOST TARGET binding site found in the 5' untranslated



region of mRNA encoded by FLJ22037, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22037 BINDING SITE, designated SEQ ID:45074, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54105] Another function of VGAM1586 is therefore inhibition of FLJ22037 (Accession XM\_168215). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22037. KIAA0564 (Accession XM\_038664) is another VGAM1586 host target gene. KIAA0564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0564 BINDING SITE, designated SEQ ID:32899, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54106] Another function of VGAM1586 is therefore inhibition of KIAA0564 (Accession XM\_038664). Accordingly, utilities

of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0564. KIAA0694 (Accession XM\_051970) is another VGAM1586 host target gene. KIAA0694 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0694 BINDING SITE, designated SEQ ID:35929, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54107] Another function of VGAM1586 is therefore inhibition of KIAA0694 (Accession XM\_051970). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0694. P15-2 (Accession NM\_018698) is another VGAM1586 host target gene. P15-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P15-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P15-2 BINDING SITE,

designated SEQ ID:20781, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54108] Another function of VGAM1586 is therefore inhibition of P15-2 (Accession NM\_018698). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P15-2. Phytoceramidase, Alkaline (PHCA, Accession NM\_018367) is another VGAM1586 host target gene. PHCA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHCA BINDING SITE, designated SEQ ID:20375, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54109] Another function of VGAM1586 is therefore inhibition of Phytoceramidase, Alkaline (PHCA, Accession NM\_018367). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHCA. LOC196549 (Accession NM\_145293) is another VGAM1586 host target gene.

LOC196549 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196549 BINDING SITE, designated SEQ ID:29807, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54110] Another function of VGAM1586 is therefore inhibition of LOC196549 (Accession NM\_145293). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196549. LOC221477 (Accession XM\_166397) is another VGAM1586 host target gene. LOC221477 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221477 BINDING SITE, designated SEQ ID:44248, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54111] Another function of VGAM1586 is therefore inhibition of LOC221477 (Accession XM\_166397). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221477. LOC257017 (Accession XM\_173227) is another VGAM1586 host target gene. LOC257017 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257017 BINDING SITE, designated SEQ ID:46490, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54112] Another function of VGAM1586 is therefore inhibition of LOC257017 (Accession XM\_173227). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257017. LOC257117 (Accession XM\_171238) is another VGAM1586 host target gene. LOC257117 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257117, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257117 BINDING SITE, designated SEQ ID:46024, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54113] Another function of VGAM1586 is therefore inhibition of LOC257117 (Accession XM\_171238). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257117. LOC92973 (Accession XM\_048529) is another VGAM1586 host target gene. LOC92973 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92973, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92973 BINDING SITE, designated SEQ ID:35181, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54114] Another function of VGAM1586 is therefore inhibition of LOC92973 (Accession XM\_048529). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC92973. LOC93550 (Accession XM\_051999) is another VGAM1586 host target gene. LOC93550 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93550, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93550 BINDING SITE, designated SEQ ID:35931, to the nucleotide sequence of VGAM1586 RNA, herein designated VGAM RNA, also designated SEQ ID:4297.

[54115] Another function of VGAM1586 is therefore inhibition of LOC93550 (Accession XM\_051999). Accordingly, utilities of VGAM1586 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93550. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1587 (VGAM1587) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54116] VGAM1587 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1587 was detected is described hereinabove with reference to Figs. 1–8.

[54117] VGAM1587 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1587 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54118] VGAM1587 gene encodes a VGAM1587 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1587 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1587 precursor RNA is designated SEQ ID:1573, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1573 is located at position 93438 relative to the genome of Saimiriine Herpesvirus 2.

[54119] VGAM1587 precursor RNA folds onto itself, forming VGAM1587 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide



sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54120] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1587 folded precursor RNA into VGAM1587 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1587 RNA is designated SEQ ID:4298, and is provided hereinbelow with reference to the sequence listing part.

[54121] VGAM1587 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1587 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1587 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54122] VGAM1587 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1587 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1587 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1587 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1587 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[54123] The complementary binding of VGAM1587 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1587 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1587 host target RNA into VGAM1587 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54124] It is appreciated that VGAM1587 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1587 host target genes. The mRNA of each one of this plurality of VGAM1587 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1587 RNA, herein designated VGAM RNA, and which when bound by VGAM1587 RNA causes inhibition of translation of respective one or more VGAM1587 host target proteins.

[54125] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1587 gene, herein designated VGAM GENE, on one or more VGAM1587 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54126] It is yet further appreciated that a function of VGAM1587 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1587 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1587 correlate with, and may be deduced from, the identity of the host target genes which VGAM1587 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54127] Nucleotide sequences of the VGAM1587 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1587 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1587 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1587 are further described hereinbelow with reference to Table 1.

[54128] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1587 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1587 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54129] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1587 gene, herein designated VGAM is inhibition of expression of VGAM1587 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1587 correlate with, and may be deduced from, the identity of the target genes which VGAM1587 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54130] Ceroid-lipofuscinosis, Neuronal 2, Late Infantile (Jansky-Bielschowsky disease) (CLN2, Accession NM\_000391) is a VGAM1587 host target gene. CLN2 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by CLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN2 BINDING SITE, designated SEQ ID:5962, to the nucleotide sequence of VGAM1587 RNA, herein designated VGAM RNA, also designated SEQ ID:4298.

[54131] A function of VGAM1587 is therefore inhibition of Ceroid-lipofuscinosis, Neuronal 2, Late Infantile (Jansky-Bielschowsky disease) (CLN2, Accession NM\_000391). Accordingly, utilities of VGAM1587 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN2. Mannan-binding Lectin Serine Protease 1 (C4/C2 activating component of Ra-reactive factor) (MASP1, Accession NM\_139125) is another VGAM1587 host target gene. MASP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MASP1 BINDING SITE, designated SEQ ID:29158, to the nucleotide sequence of VGAM1587 RNA, herein designated VGAM RNA,

also designated SEQ ID:4298.

[54132] Another function of VGAM1587 is therefore inhibition of Mannan-binding Lectin Serine Protease 1 (C4/C2 activating component of Ra-reactive factor) (MASP1, Accession NM\_139125), a gene which a complement-dependent bactericidal factor . Accordingly, utilities of VGAM1587 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MASP1. The function of MASP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM566. RAS P21 Protein Activator (GTPase activating protein) 1 (RASA1, Accession NM\_022650) is another VGAM1587 host target gene. RASA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASA1 BINDING SITE, designated SEQ ID:22905, to the nucleotide sequence of VGAM1587 RNA, herein designated VGAM RNA, also designated SEQ ID:4298.

[54133] Another function of VGAM1587 is therefore inhibition of

RAS P21 Protein Activator (GTPase activating protein) 1 (RASA1, Accession NM\_022650), a gene which is involved in the control of cellular proliferation and differentiation. Accordingly, utilities of VGAM1587 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASA1. The function of RASA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM464.FXYD Domain Containing Ion Transport Regulator 3 (FXYD3, Accession NM\_021910) is another VGAM1587 host target gene. FXYD3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FXYD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FXYD3 BINDING SITE, designated SEQ ID:22434, to the nucleotide sequence of VGAM1587 RNA, herein designated VGAM RNA, also designated SEQ ID:4298.

[54134] Another function of VGAM1587 is therefore inhibition of FXYD Domain Containing Ion Transport Regulator 3 (FXYD3, Accession NM\_021910). Accordingly, utilities of



VGAM1587 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FXD3. KIAA0555 (Accession NM\_014790) is another VGAM1587 host target gene. KIAA0555 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0555, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0555 BINDING SITE, designated SEQ ID:16680, to the nucleotide sequence of VGAM1587 RNA, herein designated VGAM RNA, also designated SEQ ID:4298.

[54135] Another function of VGAM1587 is therefore inhibition of KIAA0555 (Accession NM\_014790). Accordingly, utilities of VGAM1587 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0555. KIAA0738 (Accession NM\_014719) is another VGAM1587 host target gene. KIAA0738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0738 BINDING SITE, designated SEQ ID:16278, to the nucleotide sequence of VGAM1587 RNA, herein designated VGAM RNA, also designated SEQ ID:4298.

[54136] Another function of VGAM1587 is therefore inhibition of KIAA0738 (Accession NM\_014719). Accordingly, utilities of VGAM1587 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0738. PRO2086 (Accession NM\_014111) is another VGAM1587 host target gene. PRO2086 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO2086, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2086 BINDING SITE, designated SEQ ID:15345, to the nucleotide sequence of VGAM1587 RNA, herein designated VGAM RNA, also designated SEQ ID:4298.

[54137] Another function of VGAM1587 is therefore inhibition of PRO2086 (Accession NM\_014111). Accordingly, utilities of VGAM1587 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2086. LOC253955 (Accession XM\_170486) is another VGAM1587 host target gene. LOC253955 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC253955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253955 BINDING SITE, designated SEQ ID:45326, to the nucleotide sequence of VGAM1587 RNA, herein designated VGAM RNA, also designated SEQ ID:4298.

[54138] Another function of VGAM1587 is therefore inhibition of LOC253955 (Accession XM\_170486). Accordingly, utilities of VGAM1587 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253955. LOC51696 (Accession NM\_016217) is another VGAM1587 host target gene. LOC51696 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51696 BINDING SITE, designated SEQ ID:18307, to the nucleotide sequence of VGAM1587 RNA, herein designated VGAM RNA, also designated SEQ ID:4298.

[54139] Another function of VGAM1587 is therefore inhibition of

LOC51696 (Accession NM\_016217). Accordingly, utilities of VGAM1587 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51696. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1588 (VGAM1588) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54140] VGAM1588 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1588 was detected is described hereinabove with reference to Figs. 1-8.

[54141] VGAM1588 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1588 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54142] VGAM1588 gene encodes a VGAM1588 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1588 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1588 precursor RNA is designated SEQ ID:1574, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1574 is located at position 90393 relative to the genome of Saimiriine Herpesvirus 2.

- [54143] VGAM1588 precursor RNA folds onto itself, forming VGAM1588 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54144] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1588 folded precursor RNA into VGAM1588 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide se-

quence of VGAM1588 RNA is designated SEQ ID:4299, and is provided hereinbelow with reference to the sequence listing part.

[54145] VGAM1588 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1588 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1588 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54146] VGAM1588 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1588 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1588 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1588 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1588 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54147] The complementary binding of VGAM1588 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1588 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1588 host target RNA into VGAM1588 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54148] It is appreciated that VGAM1588 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1588 host target genes. The mRNA of each one of this plurality of VGAM1588 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1588 RNA, herein designated VGAM RNA, and which when bound by VGAM1588 RNA causes inhibition of translation of respective one or more VGAM1588 host target proteins.

[54149] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1588 gene, herein designated VGAM GENE, on one or more VGAM1588 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54150] It is yet further appreciated that a function of VGAM1588



is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1588 correlate with, and may be deduced from, the identity of the host target genes which VGAM1588 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54151] Nucleotide sequences of the VGAM1588 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1588 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1588 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1588 are further described hereinbelow with reference to Table 1.

[54152] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1588 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1588 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54153] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1588 gene, herein designated VGAM is inhibition of expression of VGAM1588 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1588 correlate with, and may be deduced from, the identity of the target genes which VGAM1588 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54154] Breast Cancer 1, Early Onset (BRCA1, Accession NM\_007295) is a VGAM1588 host target gene. BRCA1 BINDING SITE1 through BRCA1 BINDING SITE10 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BRCA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRCA1 BINDING SITE1 through BRCA1 BINDING SITE10, designated SEQ ID:14169, SEQ ID:14175, SEQ ID:14181, SEQ ID:14188, SEQ ID:14194, SEQ ID:14200, SEQ ID:14208, SEQ ID:14214, SEQ ID:14220 and SEQ ID:14163 respectively, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54155] A function of VGAM1588 is therefore inhibition of Breast

Cancer 1, Early Onset (BRCA1, Accession NM\_007295). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRCA1. Isoprenylcysteine Carboxyl Methyltransferase (ICMT, Accession NM\_012405) is another VGAM1588 host target gene. ICMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICMT BINDING SITE, designated SEQ ID:14779, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54156] Another function of VGAM1588 is therefore inhibition of Isoprenylcysteine Carboxyl Methyltransferase (ICMT, Accession NM\_012405). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICMT. Interleukin 13 Receptor, Alpha 1 (IL13RA1, Accession NM\_001560) is another VGAM1588 host target gene. IL13RA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL13RA1, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL13RA1 BINDING SITE, designated SEQ ID:7283, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54157] Another function of VGAM1588 is therefore inhibition of Interleukin 13 Receptor, Alpha 1 (IL13RA1, Accession NM\_001560), a gene which binds il-13 with a low affinity. together with il-4r- alpha can form a functional receptor for il-13. Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL13RA1. The function of IL13RA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. IRTA2 (Accession NM\_031281) is another VGAM1588 host target gene. IRTA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRTA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRTA2 BINDING SITE,

designated SEQ ID:25296, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54158] Another function of VGAM1588 is therefore inhibition of IRTA2 (Accession NM\_031281), a gene which binds to the fc region of immunoglobulins gamma low affinity receptor. Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRTA2. The function of IRTA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Myosin Light Chain Kinase 2, Skeletal Muscle (MYLK2, Accession NM\_033118) is another VGAM1588 host target gene. MYLK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYLK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYLK2 BINDING SITE, designated SEQ ID:26964, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54159] Another function of VGAM1588 is therefore inhibition of Myosin Light Chain Kinase 2, Skeletal Muscle (MYLK2, Accession NM\_033118). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYLK2. Neuropeptide Y Receptor Y1 (NPY1R, Accession NM\_000909) is another VGAM1588 host target gene. NPY1R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPY1R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPY1R BINDING SITE, designated SEQ ID:6607, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54160] Another function of VGAM1588 is therefore inhibition of Neuropeptide Y Receptor Y1 (NPY1R, Accession NM\_000909), a gene which stimulates intracellular calcium flux and signals through an inhibitory G-protein. Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPY1R. The function of NPY1R has been established by previous studies. Neuropeptide Y

(NPY; 162640) is one of the most abundant neuropeptides in the mammalian nervous system and exhibits a diverse range of important physiologic activities, including effects on psychomotor activity, food intake, regulation of central endocrine secretion, and potent vasoactive effects on the cardiovascular system. Two major subtypes of NPY (Y1 and Y2) have been defined by pharmacologic criteria. The NPY Y1 receptors have been identified in a variety of tissues, including brain, spleen, small intestine, kidney, testis, placenta, and aortic smooth muscle. The Y2 receptor is found mainly in the central nervous system. Herzog et al. (1992) reported cloning of a cDNA encoding a human NPY receptor which they confirmed to be a member of the G protein-coupled receptor superfamily. When expressed in Chinese hamster ovary (CHO) or human embryonic kidney cells, the receptor exhibited characteristic ligand specificity. In the kidney cell line, the receptor was coupled to a pertussis toxin-sensitive G protein that mediated the inhibition of cyclic AMP accumulation. In the CHO cell line, on the other hand, the receptor was coupled not to inhibition of adenylate cyclase but rather to the elevation of intracellular calcium. Thus the second messenger coupling of the NPY receptor was cell type specific,

depending on the specific repertoire of G proteins and effector systems present in the cell type. Larhammar et al. (1992) independently cloned and characterized the neuropeptide Y receptor. Animal model experiments lend further support to the function of NPY1R. Naveilhan et al. (2001) generated mice deficient in NPY1R by targeted disruption. *Npy1r*  $-/-$  mice developed hyperalgesia to acute thermal, cutaneous, and visceral chemical pain, and exhibited mechanical hypersensitivity. Neuropathic pain was increased and the mice showed a complete absence of the pharmacologic analgesic effects of NPY. In the periphery, Y1 receptor activation was sufficient and required for substance P release and the subsequent development of neurogenic inflammation and plasma leakage. Naveilhan et al. (2001) concluded that the Y1 receptor is required for central physiologic and pharmacologic NPY-induced analgesia and that its activation is both sufficient and required for the release of substance P and initiation of neurogenic inflammation.

[54161] It is appreciated that the abovementioned animal model for NPY1R is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.



- [54162] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [54163] Herzog, H.; Hort, Y. J.; Ball, H. J.; Hayes, G.; Shine, J.; Selbie, L. A. : Cloned human neuropeptide Y receptor couples to two different second messenger systems. *Proc. Nat. Acad. Sci.* 89: 5794–5798, 1992. ; and
- [54164] Naveilhan, P.; Hassani, H.; Lucas, G.; Blakeman, K. H.; Hao, J.-X.; Xu, X.-J.; Wiesenfeld-Hallin, Z.; Thoren, P.; Ernfors, P. : Reduced antinociception and plasma extravasation in mice.
- [54165] Further studies establishing the function and utilities of NPY1R are found in John Hopkins OMIM database record ID 162641, and in cited publications numbered 3214–3219 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAB27A, Member RAS Oncogene Family (RAB27A, Accession NM\_004580) is another VGAM1588 host target gene. RAB27A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB27A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of RAB27A BINDING SITE, designated SEQ ID:10928, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54166] Another function of VGAM1588 is therefore inhibition of RAB27A, Member RAS Oncogene Family (RAB27A, Accession NM\_004580). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB27A. Sal-like 1 (Drosophila) (SALL1, Accession NM\_002968) is another VGAM1588 host target gene. SALL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SALL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SALL1 BINDING SITE, designated SEQ ID:8877, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54167] Another function of VGAM1588 is therefore inhibition of Sal-like 1 (Drosophila) (SALL1, Accession NM\_002968). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with SALL1. Solute Carrier Family 1 (glial high affinity glutamate transporter), Member 3 (SLC1A3, Accession NM\_004172) is another VGAM1588 host target gene. SLC1A3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SLC1A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A3 BINDING SITE, designated SEQ ID:10382, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54168] Another function of VGAM1588 is therefore inhibition of Solute Carrier Family 1 (glial high affinity glutamate transporter), Member 3 (SLC1A3, Accession NM\_004172), a gene which is a transporter molecule that regulates neurotransmitter concentrations at excitatory synapses of the mammalian cns. Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A3. The function of SLC1A3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM294.Zinc Finger Protein 134 (clone pHZ-15) (ZNF134, Accession NM\_003435) is another VGAM1588 host target gene. ZNF134 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF134 BINDING SITE, designated SEQ ID:9487, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54169] Another function of VGAM1588 is therefore inhibition of Zinc Finger Protein 134 (clone pHZ-15) (ZNF134, Accession NM\_003435). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF134. DKFZP434D193 (Accession XM\_114297) is another VGAM1588 host target gene. DKFZP434D193 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434D193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of DKFZP434D193 BINDING SITE, designated SEQ ID:42850, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54170] Another function of VGAM1588 is therefore inhibition of DKFZP434D193 (Accession XM\_114297). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434D193. DKFZp547I224 (Accession NM\_020221) is another VGAM1588 host target gene. DKFZp547I224 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp547I224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I224 BINDING SITE, designated SEQ ID:21474, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54171] Another function of VGAM1588 is therefore inhibition of DKFZp547I224 (Accession NM\_020221). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZp547I224. FLJ20514 (Accession NM\_017856) is another VGAM1588 host target gene. FLJ20514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20514 BINDING SITE, designated SEQ ID:19534, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54172] Another function of VGAM1588 is therefore inhibition of FLJ20514 (Accession NM\_017856). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20514. FLJ32332 (Accession NM\_144641) is another VGAM1588 host target gene. FLJ32332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32332 BINDING SITE, designated SEQ ID:29468, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM

RNA, also designated SEQ ID:4299.

[54173] Another function of VGAM1588 is therefore inhibition of FLJ32332 (Accession NM\_144641). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32332. KIAA1349 (Accession XM\_047617) is another VGAM1588 host target gene. KIAA1349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1349 BINDING SITE, designated SEQ ID:35013, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54174] Another function of VGAM1588 is therefore inhibition of KIAA1349 (Accession XM\_047617). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1349. KIAA1918 (Accession XM\_054951) is another VGAM1588 host target gene. KIAA1918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1918, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1918 BINDING SITE, designated SEQ ID:36214, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54175] Another function of VGAM1588 is therefore inhibition of KIAA1918 (Accession XM\_054951). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1918. Synaptotagmin-like 2 (SYTL2, Accession NM\_032943) is another VGAM1588 host target gene. SYTL2 BINDING SITE1 and SYTL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SYTL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYTL2 BINDING SITE1 and SYTL2 BINDING SITE2, designated SEQ ID:26758 and SEQ ID:26174 respectively, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54176] Another function of VGAM1588 is therefore inhibition of



Synaptotagmin-like 2 (SYTL2, Accession NM\_032943). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYTL2. LOC125704 (Accession XM\_058931) is another VGAM1588 host target gene. LOC125704 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC125704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC125704 BINDING SITE, designated SEQ ID:36798, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54177] Another function of VGAM1588 is therefore inhibition of LOC125704 (Accession XM\_058931). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC125704. LOC221738 (Accession XM\_168097) is another VGAM1588 host target gene. LOC221738 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221738, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221738 BINDING SITE, designated SEQ ID:45028, to the nucleotide sequence of VGAM1588 RNA, herein designated VGAM RNA, also designated SEQ ID:4299.

[54178] Another function of VGAM1588 is therefore inhibition of LOC221738 (Accession XM\_168097). Accordingly, utilities of VGAM1588 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221738. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1589 (VGAM1589) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54179] VGAM1589 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1589 was detected is described hereinabove with reference to Figs. 1-8.

[54180] VGAM1589 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline Herpesvirus 3. VGAM1589 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[54181] VGAM1589 gene encodes a VGAM1589 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1589 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1589 precursor RNA is designated SEQ ID:1575, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1575 is located at position 88982 relative to the genome of Ateline Herpesvirus 3.

[54182] VGAM1589 precursor RNA folds onto itself, forming VGAM1589 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54183] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1589 folded precursor RNA into VGAM1589

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1589 RNA is designated SEQ ID:4300, and is provided hereinbelow with reference to the sequence listing part.

[54184] VGAM1589 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1589 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1589 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54185] VGAM1589 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1589 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1589 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1589 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1589 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54186] The complementary binding of VGAM1589 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1589 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1589 host target RNA into VGAM1589 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[54187] It is appreciated that VGAM1589 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1589 host target genes. The mRNA of each one of this plurality of VGAM1589 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1589 RNA, herein designated VGAM RNA, and which when bound by VGAM1589 RNA causes inhibition of translation of respective one or more VGAM1589 host target proteins.

[54188] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1589 gene, herein designated VGAM GENE, on one or more VGAM1589 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54189] It is yet further appreciated that a function of VGAM1589 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1589 include diagnosis, prevention and treatment of viral infection by Ateline Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1589 correlate with, and may be deduced from, the identity of the host target genes which VGAM1589 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54190] Nucleotide sequences of the VGAM1589 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1589 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1589 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1589 are further described hereinbelow with reference to Table 1.

[54191] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1589 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1589 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54192] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1589 gene, herein designated VGAM is inhibition of expression of VGAM1589 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1589 correlate with, and may be deduced from, the identity of the target genes which VGAM1589 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54193] Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM\_114147) is a VGAM1589 host target gene. EIF1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF1A BINDING SITE, designated SEQ ID:42715, to the nucleotide sequence of VGAM1589 RNA, herein designated



VGAM RNA, also designated SEQ ID:4300.

[54194] A function of VGAM1589 is therefore inhibition of Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM\_114147), a gene which seems to be required for maximal rate of protein biosynthesis. Accordingly, utilities of VGAM1589 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF1A. The function of EIF1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Lactate Dehydrogenase B (LDHB, Accession NM\_002300) is another VGAM1589 host target gene. LDHB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LDHB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDHB BINDING SITE, designated SEQ ID:8084, to the nucleotide sequence of VGAM1589 RNA, herein designated VGAM RNA, also designated SEQ ID:4300.

[54195] Another function of VGAM1589 is therefore inhibition of Lactate Dehydrogenase B (LDHB, Accession NM\_002300), a gene which causes dehydrogenation of lactate. Accord-

ingly, utilities of VGAM1589 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDHB. The function of LDHB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM273. Neurobeachin (NBEA, Accession XM\_170732) is another VGAM1589 host target gene. NBEA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NBEA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NBEA BINDING SITE, designated SEQ ID:45492, to the nucleotide sequence of VGAM1589 RNA, herein designated VGAM RNA, also designated SEQ ID:4300.

[54196] Another function of VGAM1589 is therefore inhibition of Neurobeachin (NBEA, Accession XM\_170732), a gene which may mediate protein-protein interactions. Accordingly, utilities of VGAM1589 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBEA. The function of NBEA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM459. Regenerating Islet-derived-like, Pancreatic Stone Protein-like, Pancreatic Thread Protein-like (rat) (REGL, Accession NM\_006508) is another VGAM1589 host target gene. REGL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by REGL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of REGL BINDING SITE, designated SEQ ID:13255, to the nucleotide sequence of VGAM1589 RNA, herein designated VGAM RNA, also designated SEQ ID:4300.

[54197] Another function of VGAM1589 is therefore inhibition of Regenerating Islet-derived-like, Pancreatic Stone Protein-like, Pancreatic Thread Protein-like (rat) (REGL, Accession NM\_006508), a gene which is a member of REG family with unknown function. Accordingly, utilities of VGAM1589 include diagnosis, prevention and treatment of diseases and clinical conditions associated with REGL. The function of REGL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.FLJ21934 (Accession NM\_024743) is another

VGAM1589 host target gene. FLJ21934 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21934 BINDING SITE, designated SEQ ID:24079, to the nucleotide sequence of VGAM1589 RNA, herein designated VGAM RNA, also designated SEQ ID:4300.

[54198] Another function of VGAM1589 is therefore inhibition of FLJ21934 (Accession NM\_024743). Accordingly, utilities of VGAM1589 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21934. Tripartite Motif-containing 2 (TRIM2, Accession NM\_015271) is another VGAM1589 host target gene. TRIM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM2 BINDING SITE, designated SEQ ID:17594, to the nucleotide sequence of VGAM1589 RNA, herein designated VGAM RNA, also designated SEQ

ID:4300.

[54199] Another function of VGAM1589 is therefore inhibition of Tripartite Motif-containing 2 (TRIM2, Accession NM\_015271). Accordingly, utilities of VGAM1589 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1590 (VGAM1590) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54200] VGAM1590 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1590 was detected is described hereinabove with reference to Figs. 1–8.

[54201] VGAM1590 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline Herpesvirus 3. VGAM1590 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54202] VGAM1590 gene encodes a VGAM1590 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1590 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1590 precursor RNA is designated SEQ ID:1576, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1576 is located at position 91163 relative to the genome of Ateline Herpesvirus 3.

[54203] VGAM1590 precursor RNA folds onto itself, forming VGAM1590 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54204] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1590 folded precursor RNA into VGAM1590 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1590 RNA is designated SEQ ID:4301, and is provided hereinbelow with reference to the sequence listing part.

[54205] VGAM1590 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1590 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1590 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54206] VGAM1590 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1590 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1590 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1590 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1590 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54207] The complementary binding of VGAM1590 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1590 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1590 host target RNA into VGAM1590 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54208] It is appreciated that VGAM1590 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1590 host target genes. The mRNA of



each one of this plurality of VGAM1590 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1590 RNA, herein designated VGAM RNA, and which when bound by VGAM1590 RNA causes inhibition of translation of respective one or more VGAM1590 host target proteins.

[54209] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1590 gene, herein designated VGAM GENE, on one or more VGAM1590 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[54210] It is yet further appreciated that a function of VGAM1590 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1590 include diagnosis, prevention and treatment of viral infection by Ateline Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1590 correlate with, and may be deduced from, the identity of the host target genes which VGAM1590 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54211] Nucleotide sequences of the VGAM1590 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1590 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1590 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1590 are further described hereinbelow with reference to Table 1.

[54212] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1590 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1590 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54213] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1590 gene, herein designated VGAM is inhibition of expression of VGAM1590 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1590 correlate with, and may be deduced from, the identity of the target genes which VGAM1590 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54214] EGF-like-domain, Multiple 5 (EGFL5, Accession XM\_098838) is a VGAM1590 host target gene. EGFL5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL5 BINDING SITE, designated SEQ ID:41881, to the nucleotide sequence of VGAM1590 RNA, herein designated VGAM RNA, also designated SEQ ID:4301.

[54215] A function of VGAM1590 is therefore inhibition of EGF-like-domain, Multiple 5 (EGFL5, Accession XM\_098838). Accordingly, utilities of VGAM1590 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with EGFL5. Lectin, Mannose-binding, 1 (LMAN1, Accession NM\_005570) is another VGAM1590 host target gene. LMAN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LMAN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMAN1 BINDING SITE, designated SEQ ID:12098, to the nucleotide sequence of VGAM1590 RNA, herein designated VGAM RNA, also designated SEQ ID:4301.

[54216] Another function of VGAM1590 is therefore inhibition of Lectin, Mannose-binding, 1 (LMAN1, Accession NM\_005570). Accordingly, utilities of VGAM1590 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMAN1. Parathyroid Hormone-like Hormone (PTH LH, Accession NM\_002820) is another VGAM1590 host target gene. PTH LH BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PTH LH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of PTHLH BINDING SITE, designated SEQ ID:8686, to the nucleotide sequence of VGAM1590 RNA, herein designated VGAM RNA, also designated SEQ ID:4301.

[54217] Another function of VGAM1590 is therefore inhibition of Parathyroid Hormone-like Hormone (PTHLH, Accession NM\_002820), a gene which plays a physiological role in lactation, possibly as a hormone for the mobilization and/or transfer of calcium to the milk. Accordingly, utilities of VGAM1590 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTHLH. The function of PTHLH has been established by previous studies. PTHRP is responsible for most cases of humoral hypercalcemia of malignancy. It mimics the actions of PTH because of its structural homology with PTH and its ability to bind to and signal via the PTH/PTHRP receptor in bone and kidney. PTHRP-(1-36) appears to be one of several secretory forms of PTHRP. When this peptide was given intravenously (iv) to normal volunteers, it produced the same effects as PTH-(1-34). To determine whether PTHRP-(1-36) could be used subcutaneously (sc) in humans as a diagnostic reagent to study differences between HHM and hyperparathyroidism, Henry et al. (1997)

examined whether sc PTHRP-(1-36) could affect mineral homeostasis. PTHRP-(1-36) given sc produced increases in circulating PTHRP-(1-36), reductions in serum phosphorus and the renal phosphorus threshold, increments in fractional calcium excretion and nephrogenous cAMP excretion, and increases in plasma 1,25-dihydroxyvitamin D. The authors concluded that it is feasible to use PTHRP-(1-36) in studies of HHM and hyperparathyroidism. Animal model experiments lend further support to the function of PTHLH. Philbrick et al. (1998) found that whereas PTHRP knockout mice die at birth with a chondrodystrophic phenotype, replacement of PTHRP expression in the chondrocytes of these knockout mice using a procollagen II-driven transgene resulted in the correction of the lethal skeletal abnormalities and generated animals that were effectively PTHRP-null in all sites other than cartilage. These rescued PTHRP knockout mice survived to at least 6 months of age but were small in stature and displayed a number of developmental defects, including cranial chondrodystrophy and a failure of tooth eruption. Teeth appeared to develop normally but became trapped by the surrounding bone and underwent progressive impaction. Localization of PTHRP mRNA during normal tooth

development by in situ hybridization showed increasing levels of expression in the enamel epithelium before the formation of the eruption pathway. The type 1 PTH/PTHrP receptor is expressed in both the adjacent dental mesenchyme and in alveolar bone. The replacement of PTHrP expression in the enamel epithelium with a keratin 14-driven transgene corrected the defect in bone resorption and restored the normal program of tooth eruption. PTHrP therefore represents an essential signal in the formation of the eruption pathway.

[54218] It is appreciated that the abovementioned animal model for PTHLH is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[54219] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54220] Philbrick, W. M.; Dreyer, B. E.; Nakchbandi, I. A.; Karaplis, A. C. : Parathyroid hormone-related protein is required for tooth eruption. *Proc. Nat. Acad. Sci.* 95: 11846–11851, 1998. ; and

[54221] Strewler, G. J. : The physiology of parathyroid hormone-related protein. *New Eng. J. Med.* 342: 177–185, 2000.

[54222] Further studies establishing the function and utilities of PTHLH are found in John Hopkins OMIM database record ID 168470, and in cited publications numbered 10360–10365, 1642–1643, 3914, 10359–164 and 5451–1654 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ribonucleotide Reductase M2 B (TP53 inducible) (RRM2B, Accession XM\_042096) is another VGAM1590 host target gene. RRM2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RRM2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RRM2B BINDING SITE, designated SEQ ID:33690, to the nucleotide sequence of VGAM1590 RNA, herein designated VGAM RNA, also designated SEQ ID:4301.

[54223] Another function of VGAM1590 is therefore inhibition of Ribonucleotide Reductase M2 B (TP53 inducible) (RRM2B, Accession XM\_042096). Accordingly, utilities of VGAM1590 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RRM2B. FLJ14641 (Accession NM\_032817) is another VGAM1590



host target gene. FLJ14641 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14641, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14641 BINDING SITE, designated SEQ ID:26591, to the nucleotide sequence of VGAM1590 RNA, herein designated VGAM RNA, also designated SEQ ID:4301.

[54224] Another function of VGAM1590 is therefore inhibition of FLJ14641 (Accession NM\_032817). Accordingly, utilities of VGAM1590 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14641. FLJ20373 (Accession NM\_017792) is another VGAM1590 host target gene. FLJ20373 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20373 BINDING SITE, designated SEQ ID:19427, to the nucleotide sequence of VGAM1590 RNA, herein designated VGAM RNA, also designated SEQ ID:4301.

[54225] Another function of VGAM1590 is therefore inhibition of FLJ20373 (Accession NM\_017792). Accordingly, utilities of VGAM1590 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20373. NP220 (Accession NM\_014497) is another VGAM1590 host target gene. NP220 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NP220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NP220 BINDING SITE, designated SEQ ID:15836, to the nucleotide sequence of VGAM1590 RNA, herein designated VGAM RNA, also designated SEQ ID:4301.

[54226] Another function of VGAM1590 is therefore inhibition of NP220 (Accession NM\_014497). Accordingly, utilities of VGAM1590 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NP220. LOC148894 (Accession XM\_097542) is another VGAM1590 host target gene. LOC148894 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC148894, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148894 BINDING SITE, designated SEQ ID:40916, to the nucleotide sequence of VGAM1590 RNA, herein designated VGAM RNA, also designated SEQ ID:4301.

[54227] Another function of VGAM1590 is therefore inhibition of LOC148894 (Accession XM\_097542). Accordingly, utilities of VGAM1590 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148894. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1591 (VGAM1591) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54228] VGAM1591 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1591 was detected is described hereinabove with reference to Figs. 1-8.

[54229] VGAM1591 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline Herpesvirus 3. VGAM1591 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[54230] VGAM1591 gene encodes a VGAM1591 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1591 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1591 precursor RNA is designated SEQ ID:1577, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1577 is located at position 90226 relative to the genome of Ateline Herpesvirus 3.

[54231] VGAM1591 precursor RNA folds onto itself, forming VGAM1591 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54232] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1591 folded precursor RNA into VGAM1591

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM1591 RNA is designated SEQ ID:4302, and is provided hereinbelow with reference to the sequence listing part.

[54233] VGAM1591 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1591 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1591 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54234] VGAM1591 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1591 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1591 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1591 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1591 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54235] The complementary binding of VGAM1591 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1591 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1591 host target RNA into VGAM1591 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[54236] It is appreciated that VGAM1591 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1591 host target genes. The mRNA of each one of this plurality of VGAM1591 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1591 RNA, herein designated VGAM RNA, and which when bound by VGAM1591 RNA causes inhibition of translation of respective one or more VGAM1591 host target proteins.

[54237] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1591 gene, herein designated VGAM GENE, on one or more VGAM1591 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54238] It is yet further appreciated that a function of VGAM1591 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of viral infection by Ateline Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1591 correlate with, and may be deduced from, the identity of the host target genes which VGAM1591 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54239] Nucleotide sequences of the VGAM1591 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1591 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1591 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1591 are further described hereinbelow with reference to Table 1.

[54240] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1591 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1591 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54241] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1591 gene, herein designated VGAM is inhibition of expression of VGAM1591 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1591 correlate with, and may be deduced from, the identity of the target genes which VGAM1591 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54242] Bagpipe Homeobox Homolog 1 (Drosophila) (BAPX1, Accession NM\_001189) is a VGAM1591 host target gene. BAPX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BAPX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAPX1 BINDING SITE, designated SEQ ID:6861, to the nucleotide sequence of VGAM1591 RNA, herein

designated VGAM RNA, also designated SEQ ID:4302.

[54243] A function of VGAM1591 is therefore inhibition of Bagpipe Homeobox Homolog 1 (Drosophila) (BAPX1, Accession NM\_001189), a gene which regulates gene expression, morphogenesis, and differentiation. Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAPX1. The function of BAPX1 has been established by previous studies. Yoshiura and Murray (1997) reported the sequence of the human homolog of BAPX1 and localized it to human 4p16.1 by linkage mapping on CEPH families with polymorphic markers identified from the genomic sequence near the gene. They suggested the human BAPX1 gene as a candidate gene for disorders of skeletal development that map to 4p16.1, such as Ellis–van Creveld syndrome (OMIM Ref. No. 225500). Tribioli and Lufkin (1997) cloned the BAPX1 gene by screening a human genomic placenta library with a genomic fragment of the mouse gene. The predicted 333–amino acid sequence of the human gene product had 85% overall identity to the product of the murine gene, with 100% identity in the homeodomain. By fluorescence in situ hybridization, they mapped the BAPX1 gene to 4p16.1 in a region of syntenic

homology with mouse chromosome 5 where the mouse gene had been mapped. RT-PCR analysis demonstrated that BAPX1 is expressed in embryonic tissues, particularly the limb, and at a lower level in an embryonic lung cell line. RNA in situ hybridization showed that BAPX1 is predominantly expressed in mesenchymal condensations of the fetal limb and axial skeleton, and in lateral plate mesoderm giving rise to visceral muscle. Tribioli et al. (1997) showed that expression of Bapx1 is first detectable in embryos just before axis rotation in lateral plate mesoderm (splanchnic mesoderm) adjacent to the endodermal lining of the prospective gut, and in the most newly formed somites in the region corresponding to the presclerotome, the precursor of the vertebrae. Thus, Bapx1 is one of the earliest developmental markers for the sclerotome portion of the somite and the gut mesentery. Bapx1 continues to be expressed well into organogenesis in lateral plate mesoderm surrounding the mid- and hindgut, and in essentially all cartilaginous condensations that will subsequently undergo endochondral bone formation.

[54244] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [54245] Yoshiura, K.-I.; Murray, J. C. : Sequence and chromosomal assignment of human BAPX1, a bagpipe-related gene, to 4p16.1: a candidate gene for skeletal dysplasia. *Genomics* 45: 425-428, 1997. ; and
- [54246] Tribioli, C.; Frasch, M.; Lufkin, T. : Bapx1: an evolutionary conserved homologue of the *Drosophila* bagpipe homeobox gene is expressed in splanchnic mesoderm and the embryonic skeleton.
- [54247] Further studies establishing the function and utilities of BAPX1 are found in John Hopkins OMIM database record ID 602183, and in cited publications numbered 8529-8531 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cyclin D2 (CCND2, Accession NM\_001759) is another VGAM1591 host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7517, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4302.

[54248] Another function of VGAM1591 is therefore inhibition of Cyclin D2 (CCND2, Accession NM\_001759), a gene which is essential for the control of the cell cycle at the g1/s (start) transition. Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128.DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 6 (RNA helicase, 54kDa) (DDX6, Accession NM\_004397) is another VGAM1591 host target gene. DDX6 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DDX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX6 BINDING SITE, designated SEQ ID:10646, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54249] Another function of VGAM1591 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 6 (RNA

helicase, 54kDa) (DDX6, Accession NM\_004397), a gene which is putative RNA helicases. Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX6. The function of DDX6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. Deoxyribonuclease I-like 1 (DNASE1L1, Accession NM\_006730) is another VGAM1591 host target gene. DNASE1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNASE1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNASE1L1 BINDING SITE, designated SEQ ID:13565, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54250] Another function of VGAM1591 is therefore inhibition of Deoxyribonuclease I-like 1 (DNASE1L1, Accession NM\_006730), a gene which seems to be involved in cell death. Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with DNASE1L1. The function of DNASE1L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM885. Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM\_005463) is another VGAM1591 host target gene. HNRPDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPDL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPDL BINDING SITE, designated SEQ ID:11950, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54251] Another function of VGAM1591 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM\_005463), a gene which binds to rna molecules that contain au-rich elements. Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPDL. The function of HNRPDL and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM144. Heat Shock 70kDa Protein 8 (HSPA8, Accession NM\_006597) is another VGAM1591 host target gene. HSPA8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPA8 BINDING SITE, designated SEQ ID:13370, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54252] Another function of VGAM1591 is therefore inhibition of Heat Shock 70kDa Protein 8 (HSPA8, Accession NM\_006597), a gene which acts as a chaperone. plays an important role in cells by transiently associating with nascent polypeptides to facilitate correct folding. Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPA8. The function of HSPA8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM258. Thrombomodulin



(THBD, Accession NM\_000361) is another VGAM1591 host target gene. THBD BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by THBD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THBD BINDING SITE, designated SEQ ID:5920, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54253] Another function of VGAM1591 is therefore inhibition of Thrombomodulin (THBD, Accession NM\_000361). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THBD. Chromosome 4 Open Reading Frame 6 (C4orf6, Accession NM\_005750) is another VGAM1591 host target gene. C4orf6 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C4orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C4orf6 BINDING SITE, designated SEQ ID:12310, to the nucleotide sequence of

VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54254] Another function of VGAM1591 is therefore inhibition of Chromosome 4 Open Reading Frame 6 (C4orf6, Accession NM\_005750). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C4orf6. HT002 (Accession NM\_014066) is another VGAM1591 host target gene. HT002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HT002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HT002 BINDING SITE, designated SEQ ID:15283, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54255] Another function of VGAM1591 is therefore inhibition of HT002 (Accession NM\_014066). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HT002. KIAA0775 (Accession NM\_014726) is another VGAM1591 host target gene. KIAA0775 BINDING SITE is HOST TARGET

binding site found in the 5` untranslated region of mRNA encoded by KIAA0775, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0775 BINDING SITE, designated SEQ ID:16319, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54256] Another function of VGAM1591 is therefore inhibition of KIAA0775 (Accession NM\_014726). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0775. KIAA0821 (Accession NM\_014921) is another VGAM1591 host target gene. KIAA0821 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0821, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0821 BINDING SITE, designated SEQ ID:17199, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54257] Another function of VGAM1591 is therefore inhibition of

KIAA0821 (Accession NM\_014921). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0821. KIAA1297 (Accession XM\_051005) is another VGAM1591 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35713, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54258] Another function of VGAM1591 is therefore inhibition of KIAA1297 (Accession XM\_051005). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. MGC14161 (Accession NM\_032892) is another VGAM1591 host target gene. MGC14161 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC14161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC14161 BINDING SITE, designated SEQ ID:26720, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54259] Another function of VGAM1591 is therefore inhibition of MGC14161 (Accession NM\_032892). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14161. MGC4161 (Accession NM\_024303) is another VGAM1591 host target gene. MGC4161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4161 BINDING SITE, designated SEQ ID:23595, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54260] Another function of VGAM1591 is therefore inhibition of MGC4161 (Accession NM\_024303). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4161. Proprotein Convertase Subtilisin/kexin Type 7

(PCSK7, Accession NM\_004716) is another VGAM1591 host target gene. PCSK7 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PCSK7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCSK7 BINDING SITE, designated SEQ ID:11075, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54261] Another function of VGAM1591 is therefore inhibition of Proprotein Convertase Subtilisin/kexin Type 7 (PCSK7, Accession NM\_004716). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCSK7. PRIC285 (Accession XM\_028918) is another VGAM1591 host target gene. PRIC285 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRIC285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRIC285 BINDING SITE, designated SEQ ID:30803, to the nucleotide sequence of VGAM1591 RNA,

herein designated VGAM RNA, also designated SEQ ID:4302.

[54262] Another function of VGAM1591 is therefore inhibition of PRIC285 (Accession XM\_028918). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRIC285. LOC135763 (Accession NM\_138572) is another VGAM1591 host target gene. LOC135763 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135763 BINDING SITE, designated SEQ ID:28882, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54263] Another function of VGAM1591 is therefore inhibition of LOC135763 (Accession NM\_138572). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135763. LOC149464 (Accession XM\_097645) is another VGAM1591 host target gene. LOC149464 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC149464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149464 BINDING SITE, designated SEQ ID:40992, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54264] Another function of VGAM1591 is therefore inhibition of LOC149464 (Accession XM\_097645). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149464. LOC200531 (Accession XM\_114244) is another VGAM1591 host target gene. LOC200531 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200531, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200531 BINDING SITE, designated SEQ ID:42818, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54265] Another function of VGAM1591 is therefore inhibition of LOC200531 (Accession XM\_114244). Accordingly, utilities



of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200531. LOC201689 (Accession XM\_040608) is another VGAM1591 host target gene. LOC201689 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201689, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201689 BINDING SITE, designated SEQ ID:33333, to the nucleotide sequence of VGAM1591 RNA, herein designated VGAM RNA, also designated SEQ ID:4302.

[54266] Another function of VGAM1591 is therefore inhibition of LOC201689 (Accession XM\_040608). Accordingly, utilities of VGAM1591 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201689. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1592 (VGAM1592) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54267] VGAM1592 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1592 was detected is described hereinabove with reference to Figs. 1–8.

[54268] VGAM1592 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline Herpesvirus 3. VGAM1592 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54269] VGAM1592 gene encodes a VGAM1592 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1592 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1592 precursor RNA is designated SEQ ID:1578, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1578 is located at position 89710 relative to the genome of Ateline Herpesvirus 3.

[54270] VGAM1592 precursor RNA folds onto itself, forming VGAM1592 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54271] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1592 folded precursor RNA into VGAM1592 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1592 RNA is designated SEQ ID:4303, and is provided hereinbelow with reference to the sequence listing part.

[54272] VGAM1592 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1592 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1592 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[54273] VGAM1592 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1592 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1592 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1592 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1592 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54274] The complementary binding of VGAM1592 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1592 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1592 host target RNA into VGAM1592 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54275] It is appreciated that VGAM1592 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1592 host target genes. The mRNA of each one of this plurality of VGAM1592 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1592 RNA, herein designated VGAM RNA, and which when bound by VGAM1592 RNA causes inhibition of translation of respective one or more VGAM1592 host target proteins.

[54276] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1592 gene, herein designated VGAM GENE, on one or more VGAM1592 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54277] It is yet further appreciated that a function of VGAM1592 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1592 include diagnosis, prevention and treatment of viral infection by Ateline Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1592 correlate with, and may be deduced from, the identity of the host target genes which VGAM1592 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54278] Nucleotide sequences of the VGAM1592 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1592 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1592 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1592 are further  
described hereinbelow with reference to Table 1.

[54279] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1592 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1592 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[54280] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1592 gene, herein designated VGAM is  
inhibition of expression of VGAM1592 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1592 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1592  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[54281] KIAA1560 (Accession XM\_034422) is a VGAM1592 host  
target gene. KIAA1560 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by KIAA1560, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1560 BINDING SITE, designated SEQ ID:32102, to the nucleotide sequence of VGAM1592 RNA, herein designated VGAM RNA, also designated SEQ ID:4303.

[54282] A function of VGAM1592 is therefore inhibition of KIAA1560 (Accession XM\_034422). Accordingly, utilities of VGAM1592 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1560. LANO (Accession NM\_025168) is another VGAM1592 host target gene. LANO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LANO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LANO BINDING SITE, designated SEQ ID:24805, to the nucleotide sequence of VGAM1592 RNA, herein designated VGAM RNA, also designated SEQ ID:4303.

[54283] Another function of VGAM1592 is therefore inhibition of



LANO (Accession NM\_025168). Accordingly, utilities of VGAM1592 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LANO. Roundabout Homolog 4, Magic Roundabout (Drosophila) (ROBO4, Accession NM\_019055) is another VGAM1592 host target gene. ROBO4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ROBO4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROBO4 BINDING SITE, designated SEQ ID:21133, to the nucleotide sequence of VGAM1592 RNA, herein designated VGAM RNA, also designated SEQ ID:4303.

[54284] Another function of VGAM1592 is therefore inhibition of Roundabout Homolog 4, Magic Roundabout (Drosophila) (ROBO4, Accession NM\_019055). Accordingly, utilities of VGAM1592 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROBO4. Unc-51-like Kinase 2 (C. elegans) (ULK2, Accession NM\_014683) is another VGAM1592 host target gene. ULK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ULK2,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ULK2 BINDING SITE, designated SEQ ID:16183, to the nucleotide sequence of VGAM1592 RNA, herein designated VGAM RNA, also designated SEQ ID:4303.

[54285] Another function of VGAM1592 is therefore inhibition of Unc-51-like Kinase 2 (*C. elegans*) (ULK2, Accession NM\_014683). Accordingly, utilities of VGAM1592 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ULK2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1593 (VGAM1593) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54286] VGAM1593 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1593 was detected is described hereinabove with reference to Figs. 1–8.

[54287] VGAM1593 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline Herpesvirus 3.

VGAM1593 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54288] VGAM1593 gene encodes a VGAM1593 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1593 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1593 precursor RNA is designated SEQ ID:1579, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1579 is located at position 86183 relative to the genome of Ateline Herpesvirus 3.

[54289] VGAM1593 precursor RNA folds onto itself, forming VGAM1593 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54290] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1593 folded precursor RNA into VGAM1593 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM1593 RNA is designated SEQ ID:4304, and is provided hereinbelow with reference to the sequence listing part.

[54291] VGAM1593 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1593 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1593 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54292] VGAM1593 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1593 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1593 RNA is an accurate or a partial inversed–reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1593 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1593 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54293] The complementary binding of VGAM1593 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1593 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1593 host target RNA into VGAM1593 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54294] It is appreciated that VGAM1593 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1593 host target genes. The mRNA of each one of this plurality of VGAM1593 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1593 RNA, herein designated VGAM RNA, and which when bound by VGAM1593 RNA causes inhibition of translation of respective one or more VGAM1593 host target proteins.

[54295] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1593 gene, herein designated VGAM GENE, on one or more VGAM1593 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54296] It is yet further appreciated that a function of VGAM1593 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of viral infection by Ateline Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1593 correlate with, and may be deduced from, the identity of the host target genes which VGAM1593 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54297] Nucleotide sequences of the VGAM1593 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1593 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1593 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1593 are further described hereinbelow with reference to Table 1.

[54298] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1593 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1593 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54299] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1593 gene, herein designated VGAM is inhibition of expression of VGAM1593 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1593 correlate with, and may be deduced from, the identity of the target genes which VGAM1593 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54300] ATPase, Cu++ Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM\_000052) is a VGAM1593 host target gene. ATP7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP7A BINDING SITE,



designated SEQ ID:5493, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54301] A function of VGAM1593 is therefore inhibition of ATPase, Cu++ Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM\_000052). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP7A. Faciogenital Dysplasia (Aarskog-Scott syndrome) (FGD1, Accession NM\_004463) is another VGAM1593 host target gene. FGD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGD1 BINDING SITE, designated SEQ ID:10768, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54302] Another function of VGAM1593 is therefore inhibition of Faciogenital Dysplasia (Aarskog-Scott syndrome) (FGD1, Accession NM\_004463), a gene which activates the ras-like family of rho- and rac proteins by exchanging bound

gdp for free gtp. Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGD1. The function of FGD1 has been established by previous studies. Aarskog (1970) described an X-linked disorder characterized by ocular hypertelorism, anteverted nostrils, broad upper lip, and peculiar penoscrotal relations ('saddle-bag scrotum' or 'shawl scrotum'). Affected males can reproduce. Scott (1971) emphasized the occurrence of ligamentous laxity manifest by hyperextensibility of the fingers, genu recurvatum, and flat feet. Furthermore, hypermobility in the cervical spine with anomaly of the odontoid resulted in neurologic deficit. He studied a family with 9 affected males in 5 sibships. Sugarman et al. (1973) described a kindred with 4 affected males. They emphasized the occurrence of a 'peculiar curved linear dimple inferior to the lower lip.' This and other stigmata were present in an earlier female. They favored sex-influenced autosomal dominant inheritance. Escobar and Weaver (1978) reported a patient who had features more suggestive of the Noonan syndrome than of the Aarskog syndrome. The patient, aged 28 years, also had severe macrocytic anemia refractory to iron therapy, hepatomegaly, hemochromatosis,

portal cirrhosis, and interstitial pulmonary disease. Tyrkus et al. (1980) described mother and son with Aarskog–Scott syndrome. Expression was complete in the mother. The mother and son had a reciprocal translocation between the X chromosome and chromosome 8. The breakpoint on the X was at Xq12. The mother's parents and sibs were clinically normal and the parents had normal karyotypes. Tyrkus et al. (1980) described parental exposure to ionizing radiation. They found that the Aarskog–Scott locus may be located at Xq12. The normal X chromosome in the mother was consistently inactivated. Thus the full expression in the mother was explained. Bawle et al. (1984) published definitively on the family in which a balanced X–autosome translocation was associated with Aarskog syndrome in mother and son. They placed the X chromosome breakpoint at Xq13. Noteworthy was the full expression in the mother comparable to the full expression of Duchenne muscular dystrophy (OMIM Ref. No. 310200) in women with balanced X–autosome translocations involving Xp21. The authors postulated that, as in the latter case, the break at Xq13 creating the translocation also caused a presumed de novo point mutation in the 'Aarskog gene' and that the woman had nonrandom

(preferential) inactivation of her structurally normal X. By high resolution cytogenetic studies, Rafael et al. (1992) demonstrated that the X chromosome breakpoint in the patient of Bawle et al. (1984) was located in the proximal short arm of the X chromosome rather than at Xq13. The autosomal breakpoint was 8q11 rather than 8p21.1, as previously reported. By study of somatic cell hybrids containing the der(X) chromosome by a combination of fluorescence in situ hybridization and Southern blot analysis with X-chromosome probes, Glover et al. (1993) refined the localization of the breakpoint to Xp11.21. Orrico et al. (2000) analyzed 13 unrelated patients with the clinical diagnosis of Aarskog–Scott syndrome. One patient carried an arg610-to-gln mutation (305400.0002) located in 1 of the 2 pleckstrin homology (PH) domains of the FGD1 gene. It corresponded to a highly conserved residue that had been involved in phosphoinositide binding in PH domains of other proteins. Critical missense mutations within the PH domain of the Bruton tyrosine kinase gene (BTK; 300300) result in X-linked agammaglobulinemia. Using SSCP analysis of the FGD1 gene, Schwartz et al. (2000) identified a missense mutation (305400.0003) in a familial case of Aarskog–Scott syndrome and a deletion

mutation (305400.0004) in a sporadic case. The authors were unable to detect alterations in the FGD1 gene in probands from 25 other familial cases, including the families originally described by Aarskog (1970) and Scott (1971), or in 15 sporadic cases. They suggested that mutational mechanisms not detected using standard analysis of coding sequence genomic DNA may cause the disorder.

[54303] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54304] Orrico, A.; Galli, L.; Falciani, M.; Bracci, M.; Cavaliere, M. L.; Rinaldi, M. M.; Musacchio, A.; Sorrentino, V. : A mutation in the pleckstrin homology (PH) domain of the FGD1 gene in an Italian family with faciogenital dysplasia (Aarskog–Scott syndrome). *FEBS Lett.* 478: 216–220, 2000. ; and

[54305] Schwartz, C. E.; Gillesen–Kaesbach, G.; May, M.; Cappa, M.; Gorski, J.; Steindl, K.; Neri, G. : Two novel mutations confirm FGD1 is responsible for the Aarskog syndrome. *Europ. J. Hum.*

[54306] Further studies establishing the function and utilities of FGD1 are found in John Hopkins OMIM database record ID 305400, and in cited publications numbered

10641–10644, 10966–10646, 3258, 10967–10648, 3259, 10649–10656, 10968–1067 and 10822–10826 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PAG (Accession NM\_018440) is another VGAM1593 host target gene. PAG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAG BINDING SITE, designated SEQ ID:20510, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54307] Another function of VGAM1593 is therefore inhibition of PAG (Accession NM\_018440). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAG. Sialyltransferase 1 (beta-galactoside alpha-2,6-sialyltransferase) (SIAT1, Accession NM\_003032) is another VGAM1593 host target gene. SIAT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT1 BINDING SITE, designated SEQ ID:8976, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54308] Another function of VGAM1593 is therefore inhibition of Sialyltransferase 1 (beta-galactoside alpha-2,6-sialyltransferase) (SIAT1, Accession NM\_003032), a gene which transfers sialic acid from the donor of substrate cmp- sialic acid to galactose containing acceptor substrates. Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT1. The function of SIAT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. Zinc Finger Protein 10 (KOX 1) (ZNF10, Accession NM\_015394) is another VGAM1593 host target gene. ZNF10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

ZNF10 BINDING SITE, designated SEQ ID:17696, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54309] Another function of VGAM1593 is therefore inhibition of Zinc Finger Protein 10 (KOX 1) (ZNF10, Accession NM\_015394), a gene which may function as a transcriptional regulator. Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF10. The function of ZNF10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM36. Calneuron 1 (CALN1, Accession NM\_031468) is another VGAM1593 host target gene. CALN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25518, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54310] Another function of VGAM1593 is therefore inhibition of



Calneuron 1 (CALN1, Accession NM\_031468). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. Cathepsin O (CTSO, Accession NM\_001334) is another VGAM1593 host target gene. CTSO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTSO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTSO BINDING SITE, designated SEQ ID:7017, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54311] Another function of VGAM1593 is therefore inhibition of Cathepsin O (CTSO, Accession NM\_001334). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTSO. FLJ21106 (Accession NM\_025097) is another VGAM1593 host target gene. FLJ21106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ21106 BINDING SITE, designated SEQ ID:24737, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54312] Another function of VGAM1593 is therefore inhibition of FLJ21106 (Accession NM\_025097). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21106. M96 (Accession NM\_007358) is another VGAM1593 host target gene. M96 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by M96, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of M96 BINDING SITE, designated SEQ ID:14289, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54313] Another function of VGAM1593 is therefore inhibition of M96 (Accession NM\_007358). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with M96. PRO1843 (Accession NM\_018507) is another VGAM1593

host target gene. PRO1843 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO1843, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1843 BINDING SITE, designated SEQ ID:20575, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54314] Another function of VGAM1593 is therefore inhibition of PRO1843 (Accession NM\_018507). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1843. PRO2958 (Accession NM\_018546) is another VGAM1593 host target gene. PRO2958 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO2958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2958 BINDING SITE, designated SEQ ID:20628, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54315] Another function of VGAM1593 is therefore inhibition of PRO2958 (Accession NM\_018546). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2958. LOC129676 (Accession XM\_065341) is another VGAM1593 host target gene. LOC129676 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC129676, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129676 BINDING SITE, designated SEQ ID:37290, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54316] Another function of VGAM1593 is therefore inhibition of LOC129676 (Accession XM\_065341). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129676. LOC131583 (Accession XM\_067456) is another VGAM1593 host target gene. LOC131583 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC131583, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131583 BINDING SITE, designated SEQ ID:37357, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54317] Another function of VGAM1593 is therefore inhibition of LOC131583 (Accession XM\_067456). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131583. LOC91291 (Accession XM\_037478) is another VGAM1593 host target gene. LOC91291 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91291, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91291 BINDING SITE, designated SEQ ID:32632, to the nucleotide sequence of VGAM1593 RNA, herein designated VGAM RNA, also designated SEQ ID:4304.

[54318] Another function of VGAM1593 is therefore inhibition of LOC91291 (Accession XM\_037478). Accordingly, utilities of VGAM1593 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC91291. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1594 (VGAM1594) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54319] VGAM1594 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1594 was detected is described hereinabove with reference to Figs. 1–8.

[54320] VGAM1594 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leek Yellow Stripe Potyvirus. VGAM1594 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54321] VGAM1594 gene encodes a VGAM1594 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1594 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1594 precursor RNA is designated SEQ ID:1580, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1580 is located at position 10003 relative to the genome of Leek Yellow Stripe Potyvirus.

- [54322] VGAM1594 precursor RNA folds onto itself, forming VGAM1594 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54323] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1594 folded precursor RNA into VGAM1594 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide sequence of VGAM1594 RNA is designated SEQ ID:4305, and is provided hereinbelow with reference to the sequence listing part.

[54324] VGAM1594 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1594 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1594 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54325] VGAM1594 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1594 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1594 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1594 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in



untranslated regions of a VGAM1594 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[54326] The complementary binding of VGAM1594 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1594 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1594 host target RNA into VGAM1594 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54327] It is appreciated that VGAM1594 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1594 host target genes. The mRNA of each one of this plurality of VGAM1594 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1594 RNA, herein designated VGAM RNA, and which when bound by VGAM1594 RNA causes

inhibition of translation of respective one or more VGAM1594 host target proteins.

[54328] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1594 gene, herein designated VGAM GENE, on one or more VGAM1594 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54329] It is yet further appreciated that a function of VGAM1594 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1594 include diagnosis, prevention and

treatment of viral infection by Leek Yellow Stripe Potyvirus. Specific functions, and accordingly utilities, of VGAM1594 correlate with, and may be deduced from, the identity of the host target genes which VGAM1594 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54330] Nucleotide sequences of the VGAM1594 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1594 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1594 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1594 are further described hereinbelow with reference to Table 1.

[54331] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1594 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1594 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54332] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1594 gene, herein designated VGAM is inhibition of expression of VGAM1594 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1594 correlate with, and may be deduced from, the identity of the target genes which VGAM1594 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54333] Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_030667) is a VGAM1594 host target gene. PTPRO BINDING SITE1 through PTPRO BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRO, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE1 through PTPRO BINDING SITE5, designated SEQ ID:25001, SEQ ID:25025, SEQ ID:25016, SEQ ID:8736 and SEQ ID:25007 respectively, to the nucleotide sequence of VGAM1594 RNA, herein designated VGAM RNA, also designated SEQ ID:4305.

[54334] A function of VGAM1594 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_030667), a gene which may function as a cell contact receptor that mediates and controls cell-cell signals. Accordingly, utilities of VGAM1594 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM140. Peptidoglycan Recognition Protein (PGLYRP, Accession NM\_052890) is another VGAM1594 host target gene. PGLYRP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PGLYRP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PGLYRP BINDING SITE, designated SEQ ID:27480, to the nucleotide sequence of VGAM1594 RNA, herein designated VGAM RNA, also designated SEQ ID:4305.

[54335] Another function of VGAM1594 is therefore inhibition of Peptidoglycan Recognition Protein (PGLYRP, Accession NM\_052890). Accordingly, utilities of VGAM1594 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PGLYRP. Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM\_080792) is another VGAM1594 host target

gene. PTPNS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPNS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPNS1 BINDING SITE, designated SEQ ID:28051, to the nucleotide sequence of VGAM1594 RNA, herein designated VGAM RNA, also designated SEQ ID:4305.

[54336] Another function of VGAM1594 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM\_080792). Accordingly, utilities of VGAM1594 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPNS1. LOC146540 (Accession XM\_085497) is another VGAM1594 host target gene. LOC146540 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146540 BINDING SITE, designated SEQ ID:38200, to the nucleotide sequence of VGAM1594 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4305.

[54337] Another function of VGAM1594 is therefore inhibition of LOC146540 (Accession XM\_085497). Accordingly, utilities of VGAM1594 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146540. LOC162333 (Accession XM\_102591) is another VGAM1594 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42134, to the nucleotide sequence of VGAM1594 RNA, herein designated VGAM RNA, also designated SEQ ID:4305.

[54338] Another function of VGAM1594 is therefore inhibition of LOC162333 (Accession XM\_102591). Accordingly, utilities of VGAM1594 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC92597 (Accession XM\_046066) is another VGAM1594 host target gene. LOC92597 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92597, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92597 BINDING SITE, designated SEQ ID:34672, to the nucleotide sequence of VGAM1594 RNA, herein designated VGAM RNA, also designated SEQ ID:4305.

[54339] Another function of VGAM1594 is therefore inhibition of LOC92597 (Accession XM\_046066). Accordingly, utilities of VGAM1594 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92597. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1595 (VGAM1595) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54340] VGAM1595 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1595 was detected is described hereinabove with reference to Figs. 1-8.

[54341] VGAM1595 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leek Yellow Stripe Po-



tyvirus. VGAM1595 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54342] VGAM1595 gene encodes a VGAM1595 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1595 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1595 precursor RNA is designated SEQ ID:1581, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1581 is located at position 6252 relative to the genome of Leek Yellow Stripe Potyvirus.

[54343] VGAM1595 precursor RNA folds onto itself, forming VGAM1595 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54344] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1595 folded precursor RNA into VGAM1595 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1595 RNA is designated SEQ ID:4306, and is provided hereinbelow with reference to the sequence listing part.

[54345] VGAM1595 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1595 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1595 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54346] VGAM1595 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1595 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1595 RNA is an accurate or a partial inversed–reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1595 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1595 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54347] The complementary binding of VGAM1595 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1595 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1595 host target RNA into VGAM1595 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54348] It is appreciated that VGAM1595 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1595 host target genes. The mRNA of each one of this plurality of VGAM1595 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1595 RNA, herein designated VGAM RNA, and which when bound by VGAM1595 RNA causes inhibition of translation of respective one or more VGAM1595 host target proteins.

[54349] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1595 gene, herein designated VGAM GENE, on one or more VGAM1595 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54350] It is yet further appreciated that a function of VGAM1595 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1595 include diagnosis, prevention and treatment of viral infection by Leek Yellow Stripe Potyvirus. Specific functions, and accordingly utilities, of VGAM1595 correlate with, and may be deduced from, the identity of the host target genes which VGAM1595 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54351] Nucleotide sequences of the VGAM1595 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1595 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1595 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1595 are further described hereinbelow with reference to Table 1.

[54352] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1595 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1595 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54353] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1595 gene, herein designated VGAM is inhibition of expression of VGAM1595 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1595 correlate with, and may be deduced from, the identity of the target genes which VGAM1595 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54354] Formin Homology 2 Domain Containing 2 (FHOD2, Accession XM\_057927) is a VGAM1595 host target gene. FHOD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FHOD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHOD2 BINDING SITE, designated SEQ

ID:36552, to the nucleotide sequence of VGAM1595 RNA, herein designated VGAM RNA, also designated SEQ ID:4306.

[54355] A function of VGAM1595 is therefore inhibition of Formin Homology 2 Domain Containing 2 (FHOD2, Accession XM\_057927). Accordingly, utilities of VGAM1595 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHOD2. Protocadherin 19 (PCDH19, Accession XM\_033173) is another VGAM1595 host target gene. PCDH19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH19 BINDING SITE, designated SEQ ID:31861, to the nucleotide sequence of VGAM1595 RNA, herein designated VGAM RNA, also designated SEQ ID:4306.

[54356] Another function of VGAM1595 is therefore inhibition of Protocadherin 19 (PCDH19, Accession XM\_033173). Accordingly, utilities of VGAM1595 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH19. LOC124222 (Accession

XM\_058784) is another VGAM1595 host target gene.

LOC124222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124222 BINDING SITE, designated SEQ ID:36740, to the nucleotide sequence of VGAM1595 RNA, herein designated VGAM RNA, also designated SEQ ID:4306.

[54357] Another function of VGAM1595 is therefore inhibition of LOC124222 (Accession XM\_058784). Accordingly, utilities of VGAM1595 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124222. LOC195977 (Accession XM\_113625) is another VGAM1595 host target gene. LOC195977 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC195977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC195977 BINDING SITE, designated SEQ ID:42298, to the nucleotide sequence of VGAM1595 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4306.

[54358] Another function of VGAM1595 is therefore inhibition of LOC195977 (Accession XM\_113625). Accordingly, utilities of VGAM1595 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC195977. LOC202134 (Accession XM\_117365) is another VGAM1595 host target gene. LOC202134 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202134 BINDING SITE, designated SEQ ID:43413, to the nucleotide sequence of VGAM1595 RNA, herein designated VGAM RNA, also designated SEQ ID:4306.

[54359] Another function of VGAM1595 is therefore inhibition of LOC202134 (Accession XM\_117365). Accordingly, utilities of VGAM1595 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202134. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1596 (VGAM1596) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54360] VGAM1596 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1596 was detected is described hereinabove with reference to Figs. 1–8.

[54361] VGAM1596 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leek Yellow Stripe Potyvirus. VGAM1596 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54362] VGAM1596 gene encodes a VGAM1596 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1596 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1596 precursor RNA is designated SEQ ID:1582, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1582 is located at position 3823 relative to the genome of Leek Yellow Stripe Potyvirus.

[54363] VGAM1596 precursor RNA folds onto itself, forming

VGAM1596 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54364] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1596 folded precursor RNA into VGAM1596 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1596 RNA is designated SEQ ID:4307, and is provided hereinbelow with reference to the sequence listing part.

[54365] VGAM1596 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1596 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1596 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54366] VGAM1596 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1596 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1596 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1596 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1596 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54367] The complementary binding of VGAM1596 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1596 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1596 host target RNA into VGAM1596 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54368] It is appreciated that VGAM1596 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1596 host target genes. The mRNA of each one of this plurality of VGAM1596 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1596 RNA, herein designated VGAM RNA, and which when bound by VGAM1596 RNA causes inhibition of translation of respective one or more VGAM1596 host target proteins.

[54369] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1596 gene, herein designated VGAM GENE, on one or more VGAM1596 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54370] It is yet further appreciated that a function of VGAM1596 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1596 include diagnosis, prevention and treatment of viral infection by Leek Yellow Stripe Potyvirus. Specific functions, and accordingly utilities, of VGAM1596 correlate with, and may be deduced from, the identity of the host target genes which VGAM1596 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54371] Nucleotide sequences of the VGAM1596 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1596 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1596 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1596 are further described hereinbelow with reference to Table 1.

[54372] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1596 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1596 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54373] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1596 gene, herein designated VGAM is inhibition of expression of VGAM1596 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1596 correlate with, and may be deduced from, the identity of the target genes which VGAM1596 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[54374] Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM\_096398) is a VGAM1596 host target gene. DLG5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DLG5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLG5 BINDING SITE, designated SEQ ID:40340, to the nucleotide sequence of VGAM1596 RNA, herein designated VGAM RNA, also designated SEQ ID:4307.

[54375] A function of VGAM1596 is therefore inhibition of Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM\_096398), a gene which may transmit extracellular signals to inhibit cell proliferation. Accordingly, utilities of VGAM1596 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLG5. The function of DLG5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM444. Enhancer of Zeste Homolog 1 (Drosophila) (EZH1, Accession NM\_001991) is another VGAM1596 host target gene. EZH1 BINDING SITE is HOST TARGET binding



site found in the 3` untranslated region of mRNA encoded by EZH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EZH1 BINDING SITE, designated SEQ ID:7716, to the nucleotide sequence of VGAM1596 RNA, herein designated VGAM RNA, also designated SEQ ID:4307.

[54376] Another function of VGAM1596 is therefore inhibition of Enhancer of Zeste Homolog 1 (Drosophila) (EZH1, Accession NM\_001991), a gene which may act in transcriptional regulation and heterochromatin maintenance. Accordingly, utilities of VGAM1596 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EZH1. The function of EZH1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM251. Aldehyde Dehydrogenase 5 Family, Member A1 (succinate-semialdehyde dehydrogenase) (ALDH5A1, Accession NM\_001080) is another VGAM1596 host target gene. ALDH5A1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ALDH5A1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH5A1 BINDING SITE, designated SEQ ID:6741, to the nucleotide sequence of VGAM1596 RNA, herein designated VGAM RNA, also designated SEQ ID:4307.

[54377] Another function of VGAM1596 is therefore inhibition of Aldehyde Dehydrogenase 5 Family, Member A1 (succinate-semialdehyde dehydrogenase) (ALDH5A1, Accession NM\_001080). Accordingly, utilities of VGAM1596 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH5A1. Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM\_024331) is another VGAM1596 host target gene. C20orf121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf121 BINDING SITE, designated SEQ ID:23635, to the nucleotide sequence of VGAM1596 RNA, herein designated VGAM RNA, also designated SEQ ID:4307.

[54378] Another function of VGAM1596 is therefore inhibition of Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM\_024331). Accordingly, utilities of VGAM1596 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf121. Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM\_052832) is another VGAM1596 host target gene. SLC26A7 BINDING SITE1 and SLC26A7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC26A7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A7 BINDING SITE1 and SLC26A7 BINDING SITE2, designated SEQ ID:27412 and SEQ ID:28624 respectively, to the nucleotide sequence of VGAM1596 RNA, herein designated VGAM RNA, also designated SEQ ID:4307.

[54379] Another function of VGAM1596 is therefore inhibition of Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM\_052832). Accordingly, utilities of VGAM1596 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A7. Fig. 1 further provides a conceptual description of a novel bioinformati-

cally detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1597 (VGAM1597) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54380] VGAM1597 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1597 was detected is described hereinabove with reference to Figs. 1–8.

[54381] VGAM1597 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leek Yellow Stripe Potyvirus. VGAM1597 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54382] VGAM1597 gene encodes a VGAM1597 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1597 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1597 precursor RNA is designated SEQ ID:1583, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1583 is located at position 5446 relative to the

genome of Leek Yellow Stripe Potyvirus.

[54383] VGAM1597 precursor RNA folds onto itself, forming VGAM1597 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54384] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1597 folded precursor RNA into VGAM1597 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1597 RNA is designated SEQ ID:4308, and is provided hereinbelow with reference to the sequence listing part.

[54385] VGAM1597 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1597 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1597 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54386] VGAM1597 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1597 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1597 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1597 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1597 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[54387] The complementary binding of VGAM1597 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1597 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1597 host target RNA into VGAM1597 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54388] It is appreciated that VGAM1597 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1597 host target genes. The mRNA of each one of this plurality of VGAM1597 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1597 RNA, herein designated VGAM RNA, and which when bound by VGAM1597 RNA causes inhibition of translation of respective one or more VGAM1597 host target proteins.

[54389] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1597 gene, herein designated VGAM GENE, on one or more VGAM1597 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54390] It is yet further appreciated that a function of VGAM1597 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of viral infection by Leek Yellow Stripe Potyvirus. Specific functions, and accordingly utilities, of



VGAM1597 correlate with, and may be deduced from, the identity of the host target genes which VGAM1597 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54391] Nucleotide sequences of the VGAM1597 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1597 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1597 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1597 are further described hereinbelow with reference to Table 1.

[54392] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1597 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1597 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54393] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1597 gene, herein designated VGAM is inhibition of expression of VGAM1597 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1597 correlate with, and may be deduced

from, the identity of the target genes which VGAM1597 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54394] Casein Kinase 2, Alpha 1 Polypeptide (CSNK2A1, Accession NM\_001895) is a VGAM1597 host target gene. CSNK2A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSNK2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSNK2A1 BINDING SITE, designated SEQ ID:7621, to the nucleotide sequence of VGAM1597 RNA, herein designated VGAM RNA, also designated SEQ ID:4308.

[54395] A function of VGAM1597 is therefore inhibition of Casein Kinase 2, Alpha 1 Polypeptide (CSNK2A1, Accession NM\_001895), a gene which cphosphorylates acidic protein such as casein. Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSNK2A1. The function of CSNK2A1 has been established by previous studies. Phosphorylation of the human p53 protein (OMIM Ref. No. 191170) at ser392 is responsive to ultraviolet (UV) but not

gamma irradiation. Keller et al. (2001) identified and purified a mammalian UV-activated protein kinase complex that phosphorylates ser392 in vitro. This kinase complex contains CK2 and the chromatin transcriptional elongation factor FACT, a heterodimer of SPT16 (OMIM Ref. No. 605012) and SSRP1 (OMIM Ref. No. 604328). In vitro studies showed that FACT alters the specificity of CK2 in the complex such that it selectively phosphorylates p53 over other substrates, including casein. In addition, phosphorylation by the kinase complex was found to enhance p53 activity. These results provided a potential mechanism for p53 activation by UV irradiation Doray et al. (2002) demonstrated that the Golgi-localized, gamma-ear-containing adenosine diphosphate ribosylation factor-binding proteins (GGA1, 606004 and GGA3, 606006) and the coat protein adaptor protein-1 (AP-1) complex (see OMIM Ref. No. AP1G2, 603534) colocalize in clathrin-coated buds of the trans-Golgi networks of mouse L cells and human HeLa cells. Binding studies revealed a direct interaction between the hinge domains of the GGAs and the gamma-ear domain of AP-1. Further, AP-1 contained bound casein kinase-2 that phosphorylated GGA1 and GGA3, thereby causing autoinhibition. Doray et al. (2002)

demonstrated that this autoinhibition could induce the directed transfer of mannose 6-phosphate receptors (see OMIM Ref. No. 154540) from the GGAs to AP-1. Mannose 6-phosphate receptors that were defective in binding to GGAs were poorly incorporated into adaptor protein complex containing clathrin coated vesicles. Thus, Doray et al. (2002) concluded that GGAs and the AP-1 complex interact to package mannose 6-phosphate receptors into AP-1-containing coated vesicles

[54396] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54397] Keller, D. M.; Zeng, X.; Wang, Y.; Zhang, Q. H.; Kapoor, M.; Shu, H.; Goodman, R.; Lozano, G.; Zhao, Y.; Lu, H. : A DNA damage-induced p53 serine 392 kinase complex contains CK2, hSpt16, and SSRP1. *Molec. Cell* 283-292, 2001. ; and

[54398] Doray, B.; Ghosh, P.; Griffith, J.; Geuze, H. J.; Kornfeld, S. : Cooperation of GGAs and AP-1 in packaging MPRs at the trans-Golgi network. *Science* 297: 1700-1703, 2002.

[54399] Further studies establishing the function and utilities of CSNK2A1 are found in John Hopkins OMIM database record ID 115440, and in cited publications numbered 12595-12596, 1035 and 12597-12600 listed in the bibli-

ography section hereinbelow, which are also hereby incorporated by reference. SORCS1 (Accession NM\_052918) is another VGAM1597 host target gene. SORCS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SORCS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORCS1 BINDING SITE, designated SEQ ID:27484, to the nucleotide sequence of VGAM1597 RNA, herein designated VGAM RNA, also designated SEQ ID:4308.

[54400] Another function of VGAM1597 is therefore inhibition of SORCS1 (Accession NM\_052918). Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORCS1. DKFZP564O0423 (Accession XM\_166254) is another VGAM1597 host target gene. DKFZP564O0423 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O0423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0423 BINDING SITE,

designated SEQ ID:44065, to the nucleotide sequence of VGAM1597 RNA, herein designated VGAM RNA, also designated SEQ ID:4308.

[54401] Another function of VGAM1597 is therefore inhibition of DKFZP564O0423 (Accession XM\_166254). Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0423. DKFZP586J0619 (Accession XM\_088280) is another VGAM1597 host target gene. DKFZP586J0619 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586J0619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586J0619 BINDING SITE, designated SEQ ID:39581, to the nucleotide sequence of VGAM1597 RNA, herein designated VGAM RNA, also designated SEQ ID:4308.

[54402] Another function of VGAM1597 is therefore inhibition of DKFZP586J0619 (Accession XM\_088280). Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586J0619. GFR (Accession NM\_012294) is an-

other VGAM1597 host target gene. GFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFR BINDING SITE, designated SEQ ID:14637, to the nucleotide sequence of VGAM1597 RNA, herein designated VGAM RNA, also designated SEQ ID:4308.

[54403] Another function of VGAM1597 is therefore inhibition of GFR (Accession NM\_012294). Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFR. KIAA0429 (Accession NM\_014751) is another VGAM1597 host target gene. KIAA0429 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0429 BINDING SITE, designated SEQ ID:16466, to the nucleotide sequence of VGAM1597 RNA, herein designated VGAM RNA, also designated SEQ ID:4308.

[54404] Another function of VGAM1597 is therefore inhibition of KIAA0429 (Accession NM\_014751). Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0429. MGC11115 (Accession NM\_032310) is another VGAM1597 host target gene. MGC11115 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11115, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11115 BINDING SITE, designated SEQ ID:26093, to the nucleotide sequence of VGAM1597 RNA, herein designated VGAM RNA, also designated SEQ ID:4308.

[54405] Another function of VGAM1597 is therefore inhibition of MGC11115 (Accession NM\_032310). Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11115. LOC151391 (Accession XM\_098050) is another VGAM1597 host target gene. LOC151391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151391, corresponding to a HOST TARGET binding site such as BIND-



ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151391 BINDING SITE, designated SEQ ID:41336, to the nucleotide sequence of VGAM1597 RNA, herein designated VGAM RNA, also designated SEQ ID:4308.

[54406] Another function of VGAM1597 is therefore inhibition of LOC151391 (Accession XM\_098050). Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151391. LOC163882 (Accession XM\_089211) is another VGAM1597 host target gene. LOC163882 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC163882, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163882 BINDING SITE, designated SEQ ID:39972, to the nucleotide sequence of VGAM1597 RNA, herein designated VGAM RNA, also designated SEQ ID:4308.

[54407] Another function of VGAM1597 is therefore inhibition of LOC163882 (Accession XM\_089211). Accordingly, utilities of VGAM1597 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC163882. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1598 (VGAM1598) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54408] VGAM1598 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1598 was detected is described hereinabove with reference to Figs. 1–8.

[54409] VGAM1598 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus E. VGAM1598 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54410] VGAM1598 gene encodes a VGAM1598 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1598 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1598 precursor RNA is designated SEQ ID:1584, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1584 is located at position 32869 relative to the genome of Human Adenovirus E.

- [54411] VGAM1598 precursor RNA folds onto itself, forming VGAM1598 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54412] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1598 folded precursor RNA into VGAM1598 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1598 RNA is designated SEQ ID:4309, and is provided hereinbelow with reference to the sequence listing part.

[54413] VGAM1598 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1598 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1598 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54414] VGAM1598 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1598 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1598 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1598 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1598 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[54415] The complementary binding of VGAM1598 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1598 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1598 host target RNA into VGAM1598 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54416] It is appreciated that VGAM1598 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1598 host target genes. The mRNA of each one of this plurality of VGAM1598 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1598 RNA, herein designated VGAM RNA, and which when bound by VGAM1598 RNA causes

inhibition of translation of respective one or more VGAM1598 host target proteins.

[54417] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1598 gene, herein designated VGAM GENE, on one or more VGAM1598 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54418] It is yet further appreciated that a function of VGAM1598 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1598 include diagnosis, prevention and

treatment of viral infection by Human Adenovirus E. Specific functions, and accordingly utilities, of VGAM1598 correlate with, and may be deduced from, the identity of the host target genes which VGAM1598 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54419] Nucleotide sequences of the VGAM1598 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1598 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1598 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1598 are further described hereinbelow with reference to Table 1.

[54420] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1598 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1598 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54421] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1598 gene, herein designated VGAM is inhibition of expression of VGAM1598 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1598 correlate with, and may be deduced from, the identity of the target genes which VGAM1598 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54422] Sperm Associated Antigen 8 (SPAG8, Accession NM\_012436) is a VGAM1598 host target gene. SPAG8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPAG8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPAG8 BINDING SITE, designated SEQ ID:14816, to the nucleotide sequence of VGAM1598 RNA, herein designated VGAM RNA, also designated SEQ ID:4309.

[54423] A function of VGAM1598 is therefore inhibition of Sperm Associated Antigen 8 (SPAG8, Accession NM\_012436), a gene which is a Sperm plasma membrane antigens are attractive antifertility vaccine targets. Accordingly, utilities of VGAM1598 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPAG8. The function of SPAG8 and its association with various diseases and clinical conditions, has been estab-



lished by previous studies, as described hereinabove with reference to VGAM129.KIAA0471 (Accession NM\_014857) is another VGAM1598 host target gene. KIAA0471 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0471 BINDING SITE, designated SEQ ID:16912, to the nucleotide sequence of VGAM1598 RNA, herein designated VGAM RNA, also designated SEQ ID:4309.

[54424] Another function of VGAM1598 is therefore inhibition of KIAA0471 (Accession NM\_014857). Accordingly, utilities of VGAM1598 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0471. RAB35, Member RAS Oncogene Family (RAB35, Accession NM\_006861) is another VGAM1598 host target gene. RAB35 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB35, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB35 BINDING SITE, designated SEQ

ID:13731, to the nucleotide sequence of VGAM1598 RNA, herein designated VGAM RNA, also designated SEQ ID:4309.

[54425] Another function of VGAM1598 is therefore inhibition of RAB35, Member RAS Oncogene Family (RAB35, Accession NM\_006861). Accordingly, utilities of VGAM1598 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB35. LOC129138 (Accession NM\_138797) is another VGAM1598 host target gene. LOC129138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129138 BINDING SITE, designated SEQ ID:29018, to the nucleotide sequence of VGAM1598 RNA, herein designated VGAM RNA, also designated SEQ ID:4309.

[54426] Another function of VGAM1598 is therefore inhibition of LOC129138 (Accession NM\_138797). Accordingly, utilities of VGAM1598 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129138. LOC164955 (Accession XM\_092265) is an-

other VGAM1598 host target gene. LOC164955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164955 BINDING SITE, designated SEQ ID:40112, to the nucleotide sequence of VGAM1598 RNA, herein designated VGAM RNA, also designated SEQ ID:4309.

[54427] Another function of VGAM1598 is therefore inhibition of LOC164955 (Accession XM\_092265). Accordingly, utilities of VGAM1598 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164955. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1599 (VGAM1599) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54428] VGAM1599 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1599 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[54429] VGAM1599 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus E. VGAM1599 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54430] VGAM1599 gene encodes a VGAM1599 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1599 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1599 precursor RNA is designated SEQ ID:1585, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1585 is located at position 24788 relative to the genome of Human Adenovirus E.

[54431] VGAM1599 precursor RNA folds onto itself, forming VGAM1599 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54432] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1599 folded precursor RNA into VGAM1599 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1599 RNA is designated SEQ ID:4310, and is provided hereinbelow with reference to the sequence listing part.

[54433] VGAM1599 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1599 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1599 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54434] VGAM1599 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1599 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1599 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1599 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1599 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54435] The complementary binding of VGAM1599 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1599 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1599 host target RNA into VGAM1599 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54436] It is appreciated that VGAM1599 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1599 host target genes. The mRNA of each one of this plurality of VGAM1599 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1599 RNA, herein designated VGAM RNA, and which when bound by VGAM1599 RNA causes inhibition of translation of respective one or more VGAM1599 host target proteins.

[54437] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1599 gene, herein designated VGAM GENE, on one or more VGAM1599 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54438] It is yet further appreciated that a function of VGAM1599 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of viral infection by Human Adenovirus E. Specific functions, and accordingly utilities, of VGAM1599 correlate with, and may be deduced from, the identity of the host target genes which VGAM1599 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54439] Nucleotide sequences of the VGAM1599 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1599 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding



of VGAM1599 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1599 are further described hereinbelow with reference to Table 1.

[54440] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1599 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1599 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54441] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1599 gene, herein designated VGAM is inhibition of expression of VGAM1599 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1599 correlate with, and may be deduced from, the identity of the target genes which VGAM1599 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54442] Ankyrin 2, Neuronal (ANK2, Accession NM\_001148) is a VGAM1599 host target gene. ANK2 BINDING SITE1 and ANK2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ANK2, corresponding to HOST TARGET binding sites such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK2 BINDING SITE1 and ANK2 BINDING SITE2, designated SEQ ID:6822 and SEQ ID:21966 respectively, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54443] A function of VGAM1599 is therefore inhibition of Ankyrin 2, Neuronal (ANK2, Accession NM\_001148), a gene which attaches integral membrane proteins to cytoskeletal elements. also binds to cytoskeletal proteins. Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK2. The function of ANK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM769. Integrin, Alpha 5 (fibronectin receptor, alpha polypeptide) (ITGA5, Accession XM\_028642) is another VGAM1599 host target gene. ITGA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

ITGA5 BINDING SITE, designated SEQ ID:30721, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54444] Another function of VGAM1599 is therefore inhibition of Integrin, Alpha 5 (fibronectin receptor, alpha polypeptide) (ITGA5, Accession XM\_028642), a gene which is receptor for fibronectin and fibrinogen and recognizes the sequence r-g-d in its ligands. Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA5. The function of ITGA5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1220. Potassium Inwardly-rectifying Channel, Subfamily J, Member 5 (KCNJ5, Accession NM\_000890) is another VGAM1599 host target gene. KCNJ5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNJ5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ5 BINDING SITE, designated SEQ ID:6586, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA,

also designated SEQ ID:4310.

[54445] Another function of VGAM1599 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 5 (KCNJ5, Accession NM\_000890), a gene which is a potassium inwardly-rectifying channel. Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ5. The function of KCNJ5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM766. Leptin (obesity homolog, mouse) (LEP, Accession NM\_000230) is another VGAM1599 host target gene. LEP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEP BINDING SITE, designated SEQ ID:5735, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54446] Another function of VGAM1599 is therefore inhibition of Leptin (obesity homolog, mouse) (LEP, Accession

NM\_000230). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEP. MutS Homolog 3 (E. coli) (MSH3, Accession NM\_002439) is another VGAM1599 host target gene. MSH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSH3 BINDING SITE, designated SEQ ID:8282, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54447] Another function of VGAM1599 is therefore inhibition of MutS Homolog 3 (E. coli) (MSH3, Accession NM\_002439), a gene which belongs to the dna mismatch repair muts family. Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSH3. The function of MSH3 has been established by previous studies. Akiyama et al. (1997) screened for somatic mutations of the MSH3 (A)<sub>8</sub> repeat in 29 tumors from 23 hereditary nonpolyposis colorectal cancer patients. One or 2 A deletions in the (A)<sub>8</sub>

repeat were found in 11 (57.9%) of the 19 tumors that showed microsatellite instability (MI) but not in 10 MI-negative ones, indicating secondary mutations after germline mutations of other mismatch repair genes. Moreover, the MI frequency of 3 or more nucleotide repeats was higher in MSH3 (A)8-mutated tumor cells than in nonmutated ones. Their data suggested that a mutation of a mismatch repair gene enhances the frequency of another mismatch repair gene mutation, such as of MSH3, resulting in severe microsatellite instability. Yin et al. (1997) came to a similar conclusion: that DNA mismatch repair genes, such as MSH3 and MSH6 (OMIM Ref. No. 600678), are targets for the mutagenic activity of upstream mismatch repair gene mutations and that this enhanced genomic instability may accelerate the accumulation of mutations in replication/repair error positive tumors. Animal model experiments lend further support to the function of MSH3. De Wind et al. (1999) inactivated the mouse Msh3 and Msh6 genes by targeted disruption. Msh6-deficient mice were prone to cancer. Most animals developed lymphomas or epithelial tumors originating from the skin and uterus but only rarely from the intestine. Msh3 deficiency did not cause cancer predisposition,

but in an Msh6-deficient background, loss of Msh3 accelerated intestinal tumorigenesis. The frequency of lymphomas was not affected. Furthermore, mismatch-directed antirecombination and sensitivity to methylating agents required Msh2 and Msh6, but not Msh3. Thus, loss of mismatch repair functions specific to Msh2/Msh6 is sufficient for lymphoma development in mice, whereas predisposition to intestinal cancer requires loss of function of both Msh2/Msh6 and Msh2/Msh3.

[54448] It is appreciated that the abovementioned animal model for MSH3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[54449] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54450] Akiyama, Y.; Tsubouchi, N.; Yuasa, Y. : Frequent somatic mutations of hMSH3 with reference to microsatellite instability in hereditary nonpolyposis colorectal cancer.

Biochem. Biophys. Res. Commun. 236: 248-252, 1997. ;  
and

[54451] de Wind, N.; Dekker, M.; Claij, N.; Jansen, L.; van Klink, Y.; Radman, M.; Riggins, G.; van der Valk, M.; van't Wout, K.;

te Riele, H. : HNPCC-like cancer predisposition in mice through.

[54452] Further studies establishing the function and utilities of MSH3 are found in John Hopkins OMIM database record ID 600887, and in cited publications numbered 716 and 9925–7797 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mature T-cell Proliferation 1 (MTCP1, Accession NM\_014221) is another VGAM1599 host target gene. MTCP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MTCP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTCP1 BINDING SITE, designated SEQ ID:15485, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54453] Another function of VGAM1599 is therefore inhibition of Mature T-cell Proliferation 1 (MTCP1, Accession NM\_014221). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTCP1. RNA (guanine-7-) Methyltransferase (RNMT, Accession NM\_003799) is an-



other VGAM1599 host target gene. RNMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNMT BINDING SITE, designated SEQ ID:9881, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54454] Another function of VGAM1599 is therefore inhibition of RNA (guanine-7-) Methyltransferase (RNMT, Accession NM\_003799), a gene which catalyzes the methylation of GpppN- at the guanine N7 position. Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNMT. The function of RNMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Tumor Necrosis Factor (ligand) Superfamily, Member 4 (tax-transcriptionally activated glycoprotein 1, 34kDa) (TNFSF4, Accession NM\_003326) is another VGAM1599 host target gene. TNFSF4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by TNFSF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF4 BINDING SITE, designated SEQ ID:9328, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54455] Another function of VGAM1599 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 4 (tax-transcriptionally activated glycoprotein 1, 34kDa) (TNFSF4, Accession NM\_003326), a gene which co-stimulates t cell proliferation and cytokine production. Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFSF4. The function of TNFSF4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM463. Apolipoprotein L, 4 (APOL4, Accession NM\_030643) is another VGAM1599 host target gene. APOL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL4, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL4 BINDING SITE, designated SEQ ID:24975, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54456] Another function of VGAM1599 is therefore inhibition of Apolipoprotein L, 4 (APOL4, Accession NM\_030643). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL4. Chromosome 21 Open Reading Frame 42 (C21orf42, Accession NM\_058184) is another VGAM1599 host target gene. C21orf42 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf42 BINDING SITE, designated SEQ ID:27749, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54457] Another function of VGAM1599 is therefore inhibition of Chromosome 21 Open Reading Frame 42 (C21orf42, Ac-

cession NM\_058184). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf42. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM\_033331) is another VGAM1599 host target gene. CDC14B BINDING SITE1 and CDC14B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CDC14B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE1 and CDC14B BINDING SITE2, designated SEQ ID:27163 and SEQ ID:9759 respectively, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54458] Another function of VGAM1599 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM\_033331). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. Dedicator of Cyto-kinesis 3 (DOCK3, Accession XM\_039259) is another VGAM1599 host target gene. DOCK3 BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by DOCK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DOCK3 BINDING SITE, designated SEQ ID:33034, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54459] Another function of VGAM1599 is therefore inhibition of Dedicator of Cyto-kinesis 3 (DOCK3, Accession XM\_039259). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DOCK3. FLJ11850 (Accession NM\_022741) is another VGAM1599 host target gene. FLJ11850 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11850, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11850 BINDING SITE, designated SEQ ID:22949, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54460] Another function of VGAM1599 is therefore inhibition of FLJ11850 (Accession NM\_022741). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11850. FLJ33069 (Accession NM\_144649) is another VGAM1599 host target gene. FLJ33069 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ33069, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ33069 BINDING SITE, designated SEQ ID:29474, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54461] Another function of VGAM1599 is therefore inhibition of FLJ33069 (Accession NM\_144649). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ33069. GMPPB (Accession XM\_171044) is another VGAM1599 host target gene. GMPPB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GMPPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GMPPB BINDING SITE, designated SEQ ID:45810, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54462] Another function of VGAM1599 is therefore inhibition of GMPPB (Accession XM\_171044). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMPPB. HCA4 (Accession XM\_085287) is another VGAM1599 host target gene. HCA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA4 BINDING SITE, designated SEQ ID:38021, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54463] Another function of VGAM1599 is therefore inhibition of HCA4 (Accession XM\_085287). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCA4.

HNK-1ST (Accession NM\_004854) is another VGAM1599 host target gene. HNK-1ST BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HNK-1ST, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNK-1ST BINDING SITE, designated SEQ ID:11265, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54464] Another function of VGAM1599 is therefore inhibition of HNK-1ST (Accession NM\_004854). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNK-1ST. KIAA0618 (Accession NM\_014833) is another VGAM1599 host target gene. KIAA0618 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0618 BINDING SITE, designated SEQ ID:16833, to the nucleotide sequence of VGAM1599 RNA, herein design-



nated VGAM RNA, also designated SEQ ID:4310.

[54465] Another function of VGAM1599 is therefore inhibition of KIAA0618 (Accession NM\_014833). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0618. KIAA0763 (Accession NM\_014869) is another VGAM1599 host target gene. KIAA0763 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0763 BINDING SITE, designated SEQ ID:16965, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54466] Another function of VGAM1599 is therefore inhibition of KIAA0763 (Accession NM\_014869). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0763. KIAA1884 (Accession XM\_055539) is another VGAM1599 host target gene. KIAA1884 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1884, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1884 BINDING SITE, designated SEQ ID:36292, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54467] Another function of VGAM1599 is therefore inhibition of KIAA1884 (Accession XM\_055539). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1884. MGC13017 (Accession NM\_080656) is another VGAM1599 host target gene. MGC13017 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13017 BINDING SITE, designated SEQ ID:27944, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54468] Another function of VGAM1599 is therefore inhibition of MGC13017 (Accession NM\_080656). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC13017. MGC22805 (Accession NM\_144590) is another VGAM1599 host target gene. MGC22805 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC22805, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC22805 BINDING SITE, designated SEQ ID:29409, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54469] Another function of VGAM1599 is therefore inhibition of MGC22805 (Accession NM\_144590). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC22805. PSR (Accession XM\_036784) is another VGAM1599 host target gene. PSR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PSR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSR BINDING SITE, designated SEQ ID:32494, to the nucleotide sequence of

VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54470] Another function of VGAM1599 is therefore inhibition of PSR (Accession XM\_036784). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSR. TGFB-induced Factor 2 (TALE family homeobox) (TGIF2, Accession NM\_021809) is another VGAM1599 host target gene. TGIF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGIF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGIF2 BINDING SITE, designated SEQ ID:22363, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54471] Another function of VGAM1599 is therefore inhibition of TGFB-induced Factor 2 (TALE family homeobox) (TGIF2, Accession NM\_021809). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGIF2. Vav 3 Oncogene (VAV3, Accession NM\_006113) is another VGAM1599 host target gene. VAV3 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by VAV3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VAV3 BINDING SITE, designated SEQ ID:12757, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54472] Another function of VGAM1599 is therefore inhibition of Vav 3 Oncogene (VAV3, Accession NM\_006113). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VAV3. LOC139770 (Accession XM\_060053) is another VGAM1599 host target gene. LOC139770 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC139770, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139770 BINDING SITE, designated SEQ ID:37144, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54473] Another function of VGAM1599 is therefore inhibition of

LOC139770 (Accession XM\_060053). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139770. LOC148413 (Accession XM\_086176) is another VGAM1599 host target gene. LOC148413 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148413 BINDING SITE, designated SEQ ID:38532, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54474] Another function of VGAM1599 is therefore inhibition of LOC148413 (Accession XM\_086176). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148413. LOC154881 (Accession XM\_088063) is another VGAM1599 host target gene. LOC154881 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC154881 BINDING SITE, designated SEQ ID:39495, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54475] Another function of VGAM1599 is therefore inhibition of LOC154881 (Accession XM\_088063). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154881. LOC158376 (Accession XM\_098934) is another VGAM1599 host target gene. LOC158376 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158376, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158376 BINDING SITE, designated SEQ ID:41971, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54476] Another function of VGAM1599 is therefore inhibition of LOC158376 (Accession XM\_098934). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158376. LOC168448 (Accession XM\_095105) is an-

other VGAM1599 host target gene. LOC168448 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC168448, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168448 BINDING SITE, designated SEQ ID:40247, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54477] Another function of VGAM1599 is therefore inhibition of LOC168448 (Accession XM\_095105). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168448. LOC200772 (Accession XM\_117275) is another VGAM1599 host target gene. LOC200772 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200772 BINDING SITE, designated SEQ ID:43346, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.



[54478] Another function of VGAM1599 is therefore inhibition of LOC200772 (Accession XM\_117275). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200772. LOC220074 (Accession NM\_145309) is another VGAM1599 host target gene. LOC220074 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220074 BINDING SITE, designated SEQ ID:29823, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54479] Another function of VGAM1599 is therefore inhibition of LOC220074 (Accession NM\_145309). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220074. LOC222962 (Accession XM\_167291) is another VGAM1599 host target gene. LOC222962 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222962, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222962 BINDING SITE, designated SEQ ID:44630, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54480] Another function of VGAM1599 is therefore inhibition of LOC222962 (Accession XM\_167291). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222962. LOC256401 (Accession XM\_171149) is another VGAM1599 host target gene. LOC256401 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256401 BINDING SITE, designated SEQ ID:45945, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54481] Another function of VGAM1599 is therefore inhibition of LOC256401 (Accession XM\_171149). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC256401. LOC90408 (Accession XM\_031517) is another VGAM1599 host target gene. LOC90408 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90408 BINDING SITE, designated SEQ ID:31395, to the nucleotide sequence of VGAM1599 RNA, herein designated VGAM RNA, also designated SEQ ID:4310.

[54482] Another function of VGAM1599 is therefore inhibition of LOC90408 (Accession XM\_031517). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90408. LOC91516 (Accession XM\_038924) is another VGAM1599 host target gene. LOC91516 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91516, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91516 BINDING SITE, designated SEQ ID:32954, to the nucleotide sequence of VGAM1599 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4310.

[54483] Another function of VGAM1599 is therefore inhibition of LOC91516 (Accession XM\_038924). Accordingly, utilities of VGAM1599 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91516. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1600 (VGAM1600) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54484] VGAM1600 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1600 was detected is described hereinabove with reference to Figs. 1–8.

[54485] VGAM1600 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus E. VGAM1600 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54486] VGAM1600 gene encodes a VGAM1600 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1600 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1600 precursor RNA is designated SEQ ID:1586, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1586 is located at position 23495 relative to the genome of Human Adenovirus E.

- [54487] VGAM1600 precursor RNA folds onto itself, forming VGAM1600 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54488] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1600 folded precursor RNA into VGAM1600 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1600 RNA is designated SEQ ID:4311, and is provided hereinbelow with reference to the sequence listing part.

[54489] VGAM1600 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1600 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1600 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54490] VGAM1600 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1600 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1600 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1600 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1600 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54491] The complementary binding of VGAM1600 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1600 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1600 host target RNA into VGAM1600 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54492] It is appreciated that VGAM1600 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1600 host target genes. The mRNA of

each one of this plurality of VGAM1600 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1600 RNA, herein designated VGAM RNA, and which when bound by VGAM1600 RNA causes inhibition of translation of respective one or more VGAM1600 host target proteins.

[54493] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1600 gene, herein designated VGAM GENE, on one or more VGAM1600 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science



294,779 (2001)).

[54494] It is yet further appreciated that a function of VGAM1600 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of viral infection by Human Adenovirus E. Specific functions, and accordingly utilities, of VGAM1600 correlate with, and may be deduced from, the identity of the host target genes which VGAM1600 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54495] Nucleotide sequences of the VGAM1600 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1600 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1600 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1600 are further described hereinbelow with reference to Table 1.

[54496] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1600 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1600 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54497] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1600 gene, herein designated VGAM is inhibition of expression of VGAM1600 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1600 correlate with, and may be deduced from, the identity of the target genes which VGAM1600 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54498] Aquaporin 6, Kidney Specific (AQP6, Accession NM\_053286) is a VGAM1600 host target gene. AQP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AQP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP6 BINDING SITE, designated SEQ ID:27613, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54499] A function of VGAM1600 is therefore inhibition of Aquaporin 6, Kidney Specific (AQP6, Accession NM\_053286), a gene which participates in distinct physiologic function

such as glomerular filtration, tubular endocytosis, and acid–base metabolism. Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AQP6. The function of AQP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340. Cadherin 5, Type 2, VE–cadherin (vascular epithelium) (CDH5, Accession NM\_001795) is another VGAM1600 host target gene. CDH5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDH5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH5 BINDING SITE, designated SEQ ID:7547, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54500] Another function of VGAM1600 is therefore inhibition of Cadherin 5, Type 2, VE–cadherin (vascular epithelium) (CDH5, Accession NM\_001795), a gene which associates with alpha–catenin forming a link to the cytoskeleton. Accordingly, utilities of VGAM1600 include diagnosis, pre–

vention and treatment of diseases and clinical conditions associated with CDH5. The function of CDH5 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1342. Hormonally Upregulated Neu-associated Kinase (HUNK, Accession NM\_014586) is another VGAM1600 host target gene. HUNK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HUNK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HUNK BINDING SITE, designated SEQ ID:15946, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54501] Another function of VGAM1600 is therefore inhibition of Hormonally Upregulated Neu-associated Kinase (HUNK, Accession NM\_014586). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HUNK. Lymphotoxin Alpha (TNF superfamily, member 1) (LTA, Accession NM\_000595) is another VGAM1600 host target gene. LTA BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by LTA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LTA BINDING SITE, designated SEQ ID:6195, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54502] Another function of VGAM1600 is therefore inhibition of Lymphotoxin Alpha (TNF superfamily, member 1) (LTA, Accession NM\_000595), a gene which is a cytokine that in its homotrimeric form binds to tnfrsf1a/tnfr1, tnfrsf1b/tnfr2 and tnfrsf14/hvem. Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LTA. The function of LTA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM662.SNL (Accession NM\_003088) is another VGAM1600 host target gene. SNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of SNL BINDING SITE, designated SEQ ID:9063, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54503] Another function of VGAM1600 is therefore inhibition of SNL (Accession NM\_003088), a gene which organizes filamentous actin into bundles with a minimum of 4.1:1 actin/fascin ratio. Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNL. The function of SNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675.SORCS3 (Accession NM\_014978) is another VGAM1600 host target gene. SORCS3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SORCS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORCS3 BINDING SITE, designated SEQ ID:17364, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54504] Another function of VGAM1600 is therefore inhibition of SORCS3 (Accession NM\_014978). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORCS3. Vasoactive Intestinal Peptide Receptor 2 (VIPR2, Accession NM\_003382) is another VGAM1600 host target gene. VIPR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VIPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VIPR2 BINDING SITE, designated SEQ ID:9412, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54505] Another function of VGAM1600 is therefore inhibition of Vasoactive Intestinal Peptide Receptor 2 (VIPR2, Accession NM\_003382). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIPR2. Wingless-type MMTV Integration Site Family, Member 1 (WNT1, Accession NM\_005430) is another VGAM1600 host target gene. WNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WNT1,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT1 BINDING SITE, designated SEQ ID:11895, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54506] Another function of VGAM1600 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 1 (WNT1, Accession NM\_005430), a gene which may have a role in development of the central nervous system. Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT1. The function of WNT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381.DKFZP434P0111 (Accession XM\_041116) is another VGAM1600 host target gene. DKFZP434P0111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P0111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P0111



BINDING SITE, designated SEQ ID:33454, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54507] Another function of VGAM1600 is therefore inhibition of DKFZP434P0111 (Accession XM\_041116). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0111. DKFZp586I021 (Accession NM\_032271) is another VGAM1600 host target gene. DKFZp586I021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp586I021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586I021 BINDING SITE, designated SEQ ID:26028, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54508] Another function of VGAM1600 is therefore inhibition of DKFZp586I021 (Accession NM\_032271). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp586I021. Pyruvate Dehydrogenase Kinase,

Isoenzyme 2 (PDK2, Accession NM\_002611) is another VGAM1600 host target gene. PDK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDK2 BINDING SITE, designated SEQ ID:8475, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54509] Another function of VGAM1600 is therefore inhibition of Pyruvate Dehydrogenase Kinase, Isoenzyme 2 (PDK2, Accession NM\_002611). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDK2. REC8 (Accession NM\_005132) is another VGAM1600 host target gene. REC8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by REC8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of REC8 BINDING SITE, designated SEQ ID:11608, to the nucleotide sequence of VGAM1600 RNA, herein

designated VGAM RNA, also designated SEQ ID:4311.

[54510] Another function of VGAM1600 is therefore inhibition of REC8 (Accession NM\_005132). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with REC8. SIMRP7 (Accession XM\_166462) is another VGAM1600 host target gene. SIMRP7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIMRP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIMRP7 BINDING SITE, designated SEQ ID:44371, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54511] Another function of VGAM1600 is therefore inhibition of SIMRP7 (Accession XM\_166462). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIMRP7. Tumor Necrosis Factor (ligand) Superfamily, Member 13 (TNFSF13, Accession NM\_003808) is another VGAM1600 host target gene. TNFSF13 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by TNFSF13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF13 BINDING SITE, designated SEQ ID:9898, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54512] Another function of VGAM1600 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 13 (TNFSF13, Accession NM\_003808). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFSF13. LOC145989 (Accession XM\_004815) is another VGAM1600 host target gene. LOC145989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145989 BINDING SITE, designated SEQ ID:29951, to the nucleotide sequence of VGAM1600 RNA, herein designated VGAM RNA, also designated SEQ ID:4311.

[54513] Another function of VGAM1600 is therefore inhibition of

LOC145989 (Accession XM\_004815). Accordingly, utilities of VGAM1600 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145989. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1601 (VGAM1601) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54514] VGAM1601 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1601 was detected is described hereinabove with reference to Figs. 1-8.

[54515] VGAM1601 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus E. VGAM1601 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54516] VGAM1601 gene encodes a VGAM1601 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1601 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1601 precursor RNA is designated SEQ ID:1587, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1587 is located at position 32517 relative to the genome of Human Adenovirus E.

- [54517] VGAM1601 precursor RNA folds onto itself, forming VGAM1601 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54518] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1601 folded precursor RNA into VGAM1601 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide se-

quence of VGAM1601 RNA is designated SEQ ID:4312, and is provided hereinbelow with reference to the sequence listing part.

[54519] VGAM1601 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1601 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1601 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54520] VGAM1601 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1601 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1601 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1601 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1601 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[54521] The complementary binding of VGAM1601 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1601 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1601 host target RNA into VGAM1601 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54522] It is appreciated that VGAM1601 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1601 host target genes. The mRNA of each one of this plurality of VGAM1601 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1601 RNA, herein designated VGAM RNA, and which when bound by VGAM1601 RNA causes inhibition of translation of respective one or more VGAM1601 host target proteins.

[54523] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1601 gene, herein designated VGAM GENE, on one or more VGAM1601 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54524] It is yet further appreciated that a function of VGAM1601

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of viral infection by Human Adenovirus E. Specific functions, and accordingly utilities, of VGAM1601 correlate with, and may be deduced from, the identity of the host target genes which VGAM1601 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54525] Nucleotide sequences of the VGAM1601 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1601 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1601 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1601 are further described hereinbelow with reference to Table 1.

[54526] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1601 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1601 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54527] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1601 gene, herein designated VGAM is inhibition of expression of VGAM1601 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1601 correlate with, and may be deduced from, the identity of the target genes which VGAM1601 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54528] Chediak–Higashi Syndrome 1 (CHS1, Accession NM\_000081) is a VGAM1601 host target gene. CHS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHS1 BINDING SITE, designated SEQ ID:5527, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54529] A function of VGAM1601 is therefore inhibition of Chediak–Higashi Syndrome 1 (CHS1, Accession NM\_000081), a gene which may sort endosomal resident proteins into late multivesicular endosome. Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CHS1. The function of CHS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Desmocollin 3 (DSC3, Accession NM\_001941) is another VGAM1601 host target gene. DSC3 BINDING SITE1 and DSC3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DSC3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSC3 BINDING SITE1 and DSC3 BINDING SITE2, designated SEQ ID:7650 and SEQ ID:23661 respectively, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54530] Another function of VGAM1601 is therefore inhibition of Desmocollin 3 (DSC3, Accession NM\_001941), a gene which is a component of intercellular desmosome junctions. Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSC3. The function of DSC3 and its association with various diseases and clinical condi-

tions, has been established by previous studies, as described hereinabove with reference to VGAM230. Mitogen-activated Protein Kinase Kinase Kinase 9 (MAP3K9, Accession XM\_027237) is another VGAM1601 host target gene. MAP3K9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K9 BINDING SITE, designated SEQ ID:30459, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54531] Another function of VGAM1601 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 9 (MAP3K9, Accession XM\_027237), a gene which is a MIXED-LINEAGE KINASE 1. Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K9. The function of MAP3K9 has been established by previous studies. While protein kinases vary widely in their primary structures, each contains a catalytic domain of 250 to 300 amino acids, which includes 11 highly con-

served motifs or subdomains separated by sequences of amino acids with reduced conservation. The presence of these motifs within a newly characterized sequence is, therefore, strongly predictive of PK activity. Furthermore, specificity of a PK for phosphorylation of either tyr or ser/thr can be predicted by the sequence of 2 of the motifs (VIb and VIII) in which different residues are conserved in each class. PKs with similar substrates or modes of activation cluster into families, whose members share a higher degree of catalytic-domain sequence identity with each other than with other members of the same PK specificity class. Hanks (1991) described 10 families of ser/thr PKs and 11 families of tyr PKs. Using the polymerase chain reaction to study mRNA expressed in human epithelial tumor cells, Dorow et al. (1993) identified a member of a new family of protein kinases. The catalytic domain of these kinases had amino acid sequence similarity to both the tyr-specific and the ser/thr-specific kinase classes. Dorow et al. (1993) isolated clones representing 2 members of this new family from a human colonic epithelial cDNA library. The predicted amino acid sequence revealed that, in addition to their unusual nature of the kinase catalytic domains, they contain 2 leu/ile-zipper motifs and a

basic sequence near their C-termini. Because they possess domains associated with proteins from 2 distinct functional groups, these kinases were referred to as mixed-lineage kinases (MLK) 1 and 2. MLK1 mRNA was found to be expressed in epithelial tumor cell lines of colonic, breast, and esophageal origin. The similarity score with MLK1 varied from 73 down to 61 for the following tyr PKs; ROS (OMIM Ref. No. 165020), ABL (OMIM Ref. No. 189980), EGFR (OMIM Ref. No. 131550), SRC (OMIM Ref. No. 190090), TRK (OMIM Ref. No. 164970), PDGFR (173410, 173490), INSR (OMIM Ref. No. 147670). The similarity score with MLK1 was 63 for RAF (OMIM Ref. No. 164760) and 52 for MOS (OMIM Ref. No. 190060)

[54532] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54533] Dorow, D. S.; Devereux, L.; Dietzsch, E.; De Kretser, T. : Identification of a new family of human epithelial protein kinases containing two leucine/isoleucine-zipper domains. *Europ. J. Biochem.* 213: 701-710, 1993. ; and

[54534] Hanks, S. K. : Eukaryotic protein kinases. *Curr. Opin. Struct. Biol.* 1: 369-383, 1991.

[54535] Further studies establishing the function and utilities of

MAP3K9 are found in John Hopkins OMIM database record ID 600136, and in cited publications numbered 1587–1588 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sialidase 3 (membrane sialidase) (NEU3, Accession NM\_006656) is another VGAM1601 host target gene. NEU3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEU3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEU3 BINDING SITE, designated SEQ ID:13453, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54536] Another function of VGAM1601 is therefore inhibition of Sialidase 3 (membrane sialidase) (NEU3, Accession NM\_006656). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEU3. Nuclear Receptor Subfamily 3, Group C, Member 2 (NR3C2, Accession NM\_000901) is another VGAM1601 host target gene. NR3C2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by



NR3C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR3C2 BINDING SITE, designated SEQ ID:6597, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54537] Another function of VGAM1601 is therefore inhibition of Nuclear Receptor Subfamily 3, Group C, Member 2 (NR3C2, Accession NM\_000901), a gene which is to increase ion and water transport and thus raise extracellular fluid volume and blood pressure and lower potassium levels. Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR3C2. The function of NR3C2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM186. Protocadherin Alpha 1 (PCDHA1, Accession NM\_031411) is another VGAM1601 host target gene. PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA1, corresponding to HOST

TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2, designated SEQ ID:25380 and SEQ ID:20861 respectively, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54538] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha 1 (PCDHA1, Accession NM\_031411). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA1. Protocadherin Alpha 10 (PCDHA10, Accession NM\_031860) is another VGAM1601 host target gene. PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2, designated SEQ ID:25612 and SEQ ID:20881 respectively, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54539] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha 10 (PCDHA10, Accession NM\_031860). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA10. Protocadherin Alpha 13 (PCDHA13, Accession NM\_018904) is another VGAM1601 host target gene. PCDHA13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA13 BINDING SITE, designated SEQ ID:20902, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54540] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha 13 (PCDHA13, Accession NM\_018904). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA13. Protocadherin Alpha 2 (PCDHA2, Accession NM\_018905) is another VGAM1601 host target gene. PCDHA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PCDHA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA2 BINDING SITE, designated SEQ ID:20912, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54541] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha 2 (PCDHA2, Accession NM\_018905). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA2. Protocadherin Alpha 3 (PCDHA3, Accession NM\_018906) is another VGAM1601 host target gene. PCDHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA3 BINDING SITE, designated SEQ ID:20922, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54542] Another function of VGAM1601 is therefore inhibition of

Protocadherin Alpha 3 (PCDHA3, Accession NM\_018906). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA3. Protocadherin Alpha 4 (PCDHA4, Accession NM\_018907) is another VGAM1601 host target gene. PCDHA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA4 BINDING SITE, designated SEQ ID:20932, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54543] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha 4 (PCDHA4, Accession NM\_018907). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA4. Protocadherin Alpha 5 (PCDHA5, Accession NM\_018908) is another VGAM1601 host target gene. PCDHA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA5, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA5 BINDING SITE, designated SEQ ID:20942, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54544] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha 5 (PCDHA5, Accession NM\_018908). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA5. Protocadherin Alpha 6 (PCDHA6, Accession NM\_018909) is another VGAM1601 host target gene. PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2, designated SEQ ID:20952 and SEQ ID:25584 respectively, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54545] Another function of VGAM1601 is therefore inhibition of

Protocadherin Alpha 6 (PCDHA6, Accession NM\_018909). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA6. Protocadherin Alpha 8 (PCDHA8, Accession NM\_018911) is another VGAM1601 host target gene. PCDHA8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA8 BINDING SITE, designated SEQ ID:20972, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54546] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha 8 (PCDHA8, Accession NM\_018911). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA8. Protocadherin Alpha 9 (PCDHA9, Accession NM\_031857) is another VGAM1601 host target gene. PCDHA9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA9, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE, designated SEQ ID:25597, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54547] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM\_031857), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM\_018898) is another VGAM1601 host target gene. PCDHAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC1 BINDING SITE, designated



SEQ ID:20841, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54548] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM\_018898). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC1. Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM\_018899) is another VGAM1601 host target gene. PCDHAC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC2 BINDING SITE, designated SEQ ID:20851, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54549] Another function of VGAM1601 is therefore inhibition of Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM\_018899). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC2. HIC (Accession

XM\_041273) is another VGAM1601 host target gene. HIC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC BINDING SITE, designated SEQ ID:33492, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54550] Another function of VGAM1601 is therefore inhibition of HIC (Accession XM\_041273). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC. KIAA0648 (Accession XM\_094043) is another VGAM1601 host target gene. KIAA0648 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0648, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0648 BINDING SITE, designated SEQ ID:40219, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54551] Another function of VGAM1601 is therefore inhibition of KIAA0648 (Accession XM\_094043). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0648. SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM\_031469) is another VGAM1601 host target gene. SH3BGRL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL2 BINDING SITE, designated SEQ ID:25525, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54552] Another function of VGAM1601 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM\_031469). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BGRL2. LOC51133 (Accession NM\_016121) is another VGAM1601 host target gene. LOC51133 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC51133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51133 BINDING SITE, designated SEQ ID:18204, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54553] Another function of VGAM1601 is therefore inhibition of LOC51133 (Accession NM\_016121). Accordingly, utilities of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51133. LOC91286 (Accession XM\_037444) is another VGAM1601 host target gene. LOC91286 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91286 BINDING SITE, designated SEQ ID:32622, to the nucleotide sequence of VGAM1601 RNA, herein designated VGAM RNA, also designated SEQ ID:4312.

[54554] Another function of VGAM1601 is therefore inhibition of LOC91286 (Accession XM\_037444). Accordingly, utilities

of VGAM1601 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91286. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1602 (VGAM1602) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54555] VGAM1602 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1602 was detected is described hereinabove with reference to Figs. 1-8.

[54556] VGAM1602 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus E. VGAM1602 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54557] VGAM1602 gene encodes a VGAM1602 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1602 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1602 precursor RNA is designated SEQ ID:1588, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1588 is located at position 27497 relative to the genome of Human Adenovirus E.

- [54558] VGAM1602 precursor RNA folds onto itself, forming VGAM1602 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54559] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1602 folded precursor RNA into VGAM1602 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 90%) nucleotide sequence of VGAM1602 RNA is designated SEQ ID:4313, and

is provided hereinbelow with reference to the sequence listing part.

[54560] VGAM1602 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1602 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1602 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[54561] VGAM1602 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1602 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1602 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1602 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1602 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54562] The complementary binding of VGAM1602 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1602 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1602 host target RNA into VGAM1602 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54563] It is appreciated that VGAM1602 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1602 host target genes. The mRNA of each one of this plurality of VGAM1602 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–



plementary to VGAM1602 RNA, herein designated VGAM RNA, and which when bound by VGAM1602 RNA causes inhibition of translation of respective one or more VGAM1602 host target proteins.

[54564] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1602 gene, herein designated VGAM GENE, on one or more VGAM1602 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54565] It is yet further appreciated that a function of VGAM1602 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1602 include diagnosis, prevention and treatment of viral infection by Human Adenovirus E. Specific functions, and accordingly utilities, of VGAM1602 correlate with, and may be deduced from, the identity of the host target genes which VGAM1602 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54566] Nucleotide sequences of the VGAM1602 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1602 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1602 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1602 are further described hereinbelow with reference to Table 1.

[54567] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1602 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1602 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54568] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1602 gene, herein designated VGAM is inhibition of expression of VGAM1602 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1602 correlate with, and may be deduced from, the identity of the target genes which VGAM1602 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54569] Deoxyguanosine Kinase (DGUOK, Accession NM\_080915) is a VGAM1602 host target gene. DGUOK BINDING SITE1 and DGUOK BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DGUOK, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGUOK BINDING SITE1 and DGUOK BINDING SITE2, designated SEQ ID:28137 and SEQ ID:28140 respectively, to the nucleotide sequence of VGAM1602 RNA, herein designated VGAM RNA, also designated SEQ ID:4313.

[54570] A function of VGAM1602 is therefore inhibition of Deoxyguanosine Kinase (DGUOK, Accession NM\_080915), a gene which is deoxyguanosine kinase and mediates phosphorylation of several deoxyribonucleosides. Accordingly,

utilities of VGAM1602 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGUOK. The function of DGUOK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM121.FLJ12505 (Accession NM\_024749) is another VGAM1602 host target gene. FLJ12505 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ12505, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12505 BINDING SITE, designated SEQ ID:24091, to the nucleotide sequence of VGAM1602 RNA, herein designated VGAM RNA, also designated SEQ ID:4313.

[54571] Another function of VGAM1602 is therefore inhibition of FLJ12505 (Accession NM\_024749). Accordingly, utilities of VGAM1602 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12505. LOC147639 (Accession XM\_085822) is another VGAM1602 host target gene. LOC147639 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by LOC147639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147639 BINDING SITE, designated SEQ ID:38343, to the nucleotide sequence of VGAM1602 RNA, herein designated VGAM RNA, also designated SEQ ID:4313.

[54572] Another function of VGAM1602 is therefore inhibition of LOC147639 (Accession XM\_085822). Accordingly, utilities of VGAM1602 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147639. LOC203286 (Accession XM\_117526) is another VGAM1602 host target gene. LOC203286 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203286 BINDING SITE, designated SEQ ID:43495, to the nucleotide sequence of VGAM1602 RNA, herein designated VGAM RNA, also designated SEQ ID:4313.

[54573] Another function of VGAM1602 is therefore inhibition of LOC203286 (Accession XM\_117526). Accordingly, utilities

of VGAM1602 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203286. LOC221773 (Accession XM\_165802) is another VGAM1602 host target gene. LOC221773 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221773 BINDING SITE, designated SEQ ID:43766, to the nucleotide sequence of VGAM1602 RNA, herein designated VGAM RNA, also designated SEQ ID:4313.

[54574] Another function of VGAM1602 is therefore inhibition of LOC221773 (Accession XM\_165802). Accordingly, utilities of VGAM1602 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221773. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1603 (VGAM1603) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54575] VGAM1603 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1603 was detected is described hereinabove with reference to Figs. 1–8.

[54576] VGAM1603 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Taura Syndrome Virus. VGAM1603 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54577] VGAM1603 gene encodes a VGAM1603 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1603 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1603 precursor RNA is designated SEQ ID:1589, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1589 is located at position 4189 relative to the genome of Taura Syndrome Virus.

[54578] VGAM1603 precursor RNA folds onto itself, forming VGAM1603 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54579] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1603 folded precursor RNA into VGAM1603 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1603 RNA is designated SEQ ID:4314, and is provided hereinbelow with reference to the sequence listing part.

[54580] VGAM1603 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1603 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1603 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated



5`UTR, PROTEIN CODING and 3`UTR respectively.

[54581] VGAM1603 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1603 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1603 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1603 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1603 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54582] The complementary binding of VGAM1603 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1603 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1603 host target RNA into VGAM1603 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54583] It is appreciated that VGAM1603 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1603 host target genes. The mRNA of each one of this plurality of VGAM1603 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1603 RNA, herein designated VGAM RNA, and which when bound by VGAM1603 RNA causes inhibition of translation of respective one or more VGAM1603 host target proteins.

[54584] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1603 gene, herein designated VGAM GENE, on one or more VGAM1603 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54585] It is yet further appreciated that a function of VGAM1603 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1603 include diagnosis, prevention and treatment of viral infection by Taura Syndrome Virus. Specific functions, and accordingly utilities, of VGAM1603 correlate with, and may be deduced from, the identity of the host target genes which VGAM1603 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54586] Nucleotide sequences of the VGAM1603 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1603 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1603 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1603 are further  
described hereinbelow with reference to Table 1.

[54587] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1603 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1603 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[54588] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1603 gene, herein designated VGAM is  
inhibition of expression of VGAM1603 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1603 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1603  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[54589] Microtubule-associated Protein 1B (MAP1B, Accession  
NM\_005909) is a VGAM1603 host target gene. MAP1B

BINDING SITE1 and MAP1B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAP1B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP1B BINDING SITE1 and MAP1B BINDING SITE2, designated SEQ ID:12536 and SEQ ID:25713 respectively, to the nucleotide sequence of VGAM1603 RNA, herein designated VGAM RNA, also designated SEQ ID:4314.

[54590] A function of VGAM1603 is therefore inhibition of Microtubule-associated Protein 1B (MAP1B, Accession NM\_005909), a gene which may have a role in neuronal plasticity and brain development. Accordingly, utilities of VGAM1603 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP1B. The function of MAP1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM316. Chromosome 22 Open Reading Frame 5 (C22orf5, Accession NM\_012264) is another VGAM1603 host target gene. C22orf5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by C22orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf5 BINDING SITE, designated SEQ ID:14582, to the nucleotide sequence of VGAM1603 RNA, herein designated VGAM RNA, also designated SEQ ID:4314.

[54591] Another function of VGAM1603 is therefore inhibition of Chromosome 22 Open Reading Frame 5 (C22orf5, Accession NM\_012264). Accordingly, utilities of VGAM1603 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf5. Cell Adhesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM\_006614) is another VGAM1603 host target gene. CHL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHL1 BINDING SITE, designated SEQ ID:13389, to the nucleotide sequence of VGAM1603 RNA, herein designated VGAM RNA, also designated SEQ ID:4314.

[54592] Another function of VGAM1603 is therefore inhibition of Cell Adhesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM\_006614). Accordingly, utilities of VGAM1603 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHL1. KIAA1910 (Accession XM\_055514) is another VGAM1603 host target gene. KIAA1910 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1910 BINDING SITE, designated SEQ ID:36283, to the nucleotide sequence of VGAM1603 RNA, herein designated VGAM RNA, also designated SEQ ID:4314.

[54593] Another function of VGAM1603 is therefore inhibition of KIAA1910 (Accession XM\_055514). Accordingly, utilities of VGAM1603 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1910. Prostate Cancer Associated Protein 7 (PCANAP7, Accession XM\_167803) is another VGAM1603 host target gene. PCANAP7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by PCANAP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCANAP7 BINDING SITE, designated SEQ ID:44836, to the nucleotide sequence of VGAM1603 RNA, herein designated VGAM RNA, also designated SEQ ID:4314.

[54594] Another function of VGAM1603 is therefore inhibition of Prostate Cancer Associated Protein 7 (PCANAP7, Accession XM\_167803). Accordingly, utilities of VGAM1603 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCANAP7. Prefoldin 1 (PFDN1, Accession NM\_002622) is another VGAM1603 host target gene. PFDN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PFDN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PFDN1 BINDING SITE, designated SEQ ID:8485, to the nucleotide sequence of VGAM1603 RNA, herein designated VGAM RNA, also designated SEQ ID:4314.

[54595] Another function of VGAM1603 is therefore inhibition of



Prefoldin 1 (PFDN1, Accession NM\_002622). Accordingly, utilities of VGAM1603 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PFDN1. LOC148709 (Accession XM\_086281) is another VGAM1603 host target gene. LOC148709 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148709 BINDING SITE, designated SEQ ID:38577, to the nucleotide sequence of VGAM1603 RNA, herein designated VGAM RNA, also designated SEQ ID:4314.

[54596] Another function of VGAM1603 is therefore inhibition of LOC148709 (Accession XM\_086281). Accordingly, utilities of VGAM1603 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148709. LOC257319 (Accession XM\_171049) is another VGAM1603 host target gene. LOC257319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC257319 BINDING SITE, designated SEQ ID:45827, to the nucleotide sequence of VGAM1603 RNA, herein designated VGAM RNA, also designated SEQ ID:4314.

[54597] Another function of VGAM1603 is therefore inhibition of LOC257319 (Accession XM\_171049). Accordingly, utilities of VGAM1603 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257319. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1604 (VGAM1604) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54598] VGAM1604 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1604 was detected is described hereinabove with reference to Figs. 1–8.

[54599] VGAM1604 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Taura Syndrome Virus. VGAM1604 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[54600] VGAM1604 gene encodes a VGAM1604 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1604 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1604 precursor RNA is designated SEQ ID:1590, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1590 is located at position 2524 relative to the genome of Taura Syndrome Virus.

[54601] VGAM1604 precursor RNA folds onto itself, forming VGAM1604 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54602] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1604 folded precursor RNA into VGAM1604 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1604 RNA is designated SEQ ID:4315, and is provided hereinbelow with reference to the sequence listing part.

[54603] VGAM1604 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1604 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1604 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54604] VGAM1604 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1604 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1604 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1604 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1604 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54605] The complementary binding of VGAM1604 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1604 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1604 host target RNA into VGAM1604 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54606] It is appreciated that VGAM1604 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1604 host target genes. The mRNA of each one of this plurality of VGAM1604 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1604 RNA, herein designated VGAM RNA, and which when bound by VGAM1604 RNA causes inhibition of translation of respective one or more VGAM1604 host target proteins.

[54607] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1604 gene, herein designated VGAM GENE, on one or more VGAM1604 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54608] It is yet further appreciated that a function of VGAM1604 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1604 include diagnosis, prevention and treatment of viral infection by Taura Syndrome Virus. Specific functions, and accordingly utilities, of VGAM1604 correlate with, and may be deduced from, the identity of the host target genes which VGAM1604 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54609] Nucleotide sequences of the VGAM1604 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1604 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1604 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1604 are further described hereinbelow with reference to Table 1.

[54610] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1604 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1604 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54611] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1604 gene, herein designated VGAM is inhibition of expression of VGAM1604 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1604 correlate with, and may be deduced from, the identity of the target genes which VGAM1604 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54612] High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483) is a VGAM1604 host target gene. HMGA2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HMGA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGA2 BINDING SITE, designated SEQ ID:9573, to the nucleotide sequence of VGAM1604 RNA, herein designated VGAM RNA, also designated SEQ ID:4315.



[54613] A function of VGAM1604 is therefore inhibition of High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483), a gene which may affect transcription and cell differentiation; shares common DNA-binding motif with other HMG HMG I/Y family members. Accordingly, utilities of VGAM1604 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGA2. The function of HMGA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM\_086728) is another VGAM1604 host target gene. C20orf110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf110 BINDING SITE, designated SEQ ID:38838, to the nucleotide sequence of VGAM1604 RNA, herein designated VGAM RNA, also designated SEQ ID:4315.

[54614] Another function of VGAM1604 is therefore inhibition of Chromosome 20 Open Reading Frame 110 (C20orf110,

Accession XM\_086728). Accordingly, utilities of VGAM1604 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf110. FLJ14621 (Accession NM\_032811) is another VGAM1604 host target gene. FLJ14621 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14621, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14621 BINDING SITE, designated SEQ ID:26577, to the nucleotide sequence of VGAM1604 RNA, herein designated VGAM RNA, also designated SEQ ID:4315.

[54615] Another function of VGAM1604 is therefore inhibition of FLJ14621 (Accession NM\_032811). Accordingly, utilities of VGAM1604 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14621. Mitochondrial Ribosomal Protein S27 (MRPS27, Accession NM\_015084) is another VGAM1604 host target gene. MRPS27 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPS27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of MRPS27 BINDING SITE, designated SEQ ID:17472, to the nucleotide sequence of VGAM1604 RNA, herein designated VGAM RNA, also designated SEQ ID:4315.

[54616] Another function of VGAM1604 is therefore inhibition of Mitochondrial Ribosomal Protein S27 (MRPS27, Accession NM\_015084). Accordingly, utilities of VGAM1604 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS27. LOC152766 (Accession XM\_098263) is another VGAM1604 host target gene. LOC152766 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152766 BINDING SITE, designated SEQ ID:41553, to the nucleotide sequence of VGAM1604 RNA, herein designated VGAM RNA, also designated SEQ ID:4315.

[54617] Another function of VGAM1604 is therefore inhibition of LOC152766 (Accession XM\_098263). Accordingly, utilities of VGAM1604 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC152766. LOC257206 (Accession XM\_173136) is another VGAM1604 host target gene. LOC257206 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257206, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257206 BINDING SITE, designated SEQ ID:46385, to the nucleotide sequence of VGAM1604 RNA, herein designated VGAM RNA, also designated SEQ ID:4315.

[54618] Another function of VGAM1604 is therefore inhibition of LOC257206 (Accession XM\_173136). Accordingly, utilities of VGAM1604 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257206. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1605 (VGAM1605) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54619] VGAM1605 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1605 was detected is described hereinabove with reference to Figs. 1–8.

[54620] VGAM1605 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Taura Syndrome Virus. VGAM1605 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54621] VGAM1605 gene encodes a VGAM1605 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1605 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1605 precursor RNA is designated SEQ ID:1591, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1591 is located at position 8483 relative to the genome of Taura Syndrome Virus.

[54622] VGAM1605 precursor RNA folds onto itself, forming VGAM1605 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54623] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1605 folded precursor RNA into VGAM1605 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1605 RNA is designated SEQ ID:4316, and is provided hereinbelow with reference to the sequence listing part.

[54624] VGAM1605 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1605 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1605 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54625] VGAM1605 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1605 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1605 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1605 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1605 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54626] The complementary binding of VGAM1605 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1605 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1605 host target RNA into VGAM1605 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54627] It is appreciated that VGAM1605 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1605 host target genes. The mRNA of each one of this plurality of VGAM1605 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1605 RNA, herein designated VGAM RNA, and which when bound by VGAM1605 RNA causes inhibition of translation of respective one or more VGAM1605 host target proteins.

[54628] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1605 gene, herein designated VGAM GENE, on one or more VGAM1605 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54629] It is yet further appreciated that a function of VGAM1605 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of viral infection by Taura Syndrome Virus. Specific functions, and accordingly utilities, of VGAM1605 correlate with, and may be deduced from, the identity of the host target genes which VGAM1605 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54630] Nucleotide sequences of the VGAM1605 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1605 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1605 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1605 are further described hereinbelow with reference to Table 1.

[54631] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1605 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1605 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54632] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1605 gene, herein designated VGAM is inhibition of expression of VGAM1605 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1605 correlate with, and may be deduced from, the identity of the target genes which VGAM1605 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54633] Secretogranin III (SCG3, Accession NM\_013243) is a VGAM1605 host target gene. SCG3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by SCG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCG3 BINDING SITE, designated SEQ ID:14903, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54634] A function of VGAM1605 is therefore inhibition of Secretogranin III (SCG3, Accession NM\_013243). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCG3. Solute Carrier Family 21 (prostaglandin transporter), Member 2 (SLC21A2, Accession NM\_005630) is another VGAM1605 host target gene. SLC21A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC21A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC21A2 BINDING SITE, designated SEQ ID:12159, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54635] Another function of VGAM1605 is therefore inhibition of

Solute Carrier Family 21 (prostaglandin transporter), Member 2 (SLC21A2, Accession NM\_005630), a gene which is a Prostaglandin transporter. Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC21A2. The function of SLC21A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM83. Cylindromatosis (turban tumor syndrome) (CYLD, Accession NM\_015247) is another VGAM1605 host target gene. CYLD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYLD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYLD BINDING SITE, designated SEQ ID:17577, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54636] Another function of VGAM1605 is therefore inhibition of Cylindromatosis (turban tumor syndrome) (CYLD, Accession NM\_015247). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with CYLD. DKFZp434G179 (Accession XM\_087065) is another VGAM1605 host target gene. DKFZp434G179 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp434G179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434G179 BINDING SITE, designated SEQ ID:39042, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54637] Another function of VGAM1605 is therefore inhibition of DKFZp434G179 (Accession XM\_087065). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434G179. FLJ21168 (Accession NM\_025073) is another VGAM1605 host target gene. FLJ21168 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21168, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21168 BINDING SITE, designated SEQ ID:24673, to the

nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54638] Another function of VGAM1605 is therefore inhibition of FLJ21168 (Accession NM\_025073). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21168. MGC9753 (Accession NM\_033419) is another VGAM1605 host target gene. MGC9753 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC9753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC9753 BINDING SITE, designated SEQ ID:27244, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54639] Another function of VGAM1605 is therefore inhibition of MGC9753 (Accession NM\_033419). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC9753. PDZ Domain Containing 2 (PDZD2, Accession XM\_087705) is another VGAM1605 host target gene. PDZD2 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by PDZD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDZD2 BINDING SITE, designated SEQ ID:39395, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54640] Another function of VGAM1605 is therefore inhibition of PDZ Domain Containing 2 (PDZD2, Accession XM\_087705). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDZD2. Solute Carrier Family 17 (sodium-dependent inorganic phosphate cotransporter), Member 6 (SLC17A6, Accession NM\_020346) is another VGAM1605 host target gene. SLC17A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC17A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC17A6 BINDING SITE, designated SEQ ID:21597, to the nucleotide sequence of VGAM1605 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4316.

[54641] Another function of VGAM1605 is therefore inhibition of Solute Carrier Family 17 (sodium-dependent inorganic phosphate cotransporter), Member 6 (SLC17A6, Accession NM\_020346). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC17A6. Zinc Finger Protein 262 (ZNF262, Accession NM\_005095) is another VGAM1605 host target gene. ZNF262 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF262, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF262 BINDING SITE, designated SEQ ID:11557, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54642] Another function of VGAM1605 is therefore inhibition of Zinc Finger Protein 262 (ZNF262, Accession NM\_005095). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF262. LOC115129 (Accession XM\_055292) is another VGAM1605 host target gene.



LOC115129 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115129 BINDING SITE, designated SEQ ID:36253, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54643] Another function of VGAM1605 is therefore inhibition of LOC115129 (Accession XM\_055292). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115129. LOC149478 (Accession XM\_086536) is another VGAM1605 host target gene. LOC149478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149478 BINDING SITE, designated SEQ ID:38756, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54644] Another function of VGAM1605 is therefore inhibition of LOC149478 (Accession XM\_086536). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149478. LOC158318 (Accession XM\_098925) is another VGAM1605 host target gene. LOC158318 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158318 BINDING SITE, designated SEQ ID:41958, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54645] Another function of VGAM1605 is therefore inhibition of LOC158318 (Accession XM\_098925). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158318. LOC90784 (Accession XM\_034109) is another VGAM1605 host target gene. LOC90784 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90784, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90784 BINDING SITE, designated SEQ ID:32003, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54646] Another function of VGAM1605 is therefore inhibition of LOC90784 (Accession XM\_034109). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90784. LOC92492 (Accession XM\_045396) is another VGAM1605 host target gene. LOC92492 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92492, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92492 BINDING SITE, designated SEQ ID:34455, to the nucleotide sequence of VGAM1605 RNA, herein designated VGAM RNA, also designated SEQ ID:4316.

[54647] Another function of VGAM1605 is therefore inhibition of LOC92492 (Accession XM\_045396). Accordingly, utilities of VGAM1605 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC92492. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1606 (VGAM1606) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54648] VGAM1606 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1606 was detected is described hereinabove with reference to Figs. 1–8.

[54649] VGAM1606 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Taura Syndrome Virus. VGAM1606 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54650] VGAM1606 gene encodes a VGAM1606 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1606 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1606 precursor RNA is designated SEQ ID:1592, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1592 is located at position 7811 relative to the genome of Taura Syndrome Virus.

- [54651] VGAM1606 precursor RNA folds onto itself, forming VGAM1606 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54652] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1606 folded precursor RNA into VGAM1606 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1606 RNA is designated SEQ ID:4317, and is provided hereinbelow with reference to the sequence listing part.

[54653] VGAM1606 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1606 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1606 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[54654] VGAM1606 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1606 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1606 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1606 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1606 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[54655] The complementary binding of VGAM1606 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1606 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1606 host target RNA into VGAM1606 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54656] It is appreciated that VGAM1606 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1606 host target genes. The mRNA of each one of this plurality of VGAM1606 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1606 RNA, herein designated VGAM RNA, and which when bound by VGAM1606 RNA causes

inhibition of translation of respective one or more VGAM1606 host target proteins.

[54657] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1606 gene, herein designated VGAM GENE, on one or more VGAM1606 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54658] It is yet further appreciated that a function of VGAM1606 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1606 include diagnosis, prevention and



treatment of viral infection by Taura Syndrome Virus. Specific functions, and accordingly utilities, of VGAM1606 correlate with, and may be deduced from, the identity of the host target genes which VGAM1606 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54659] Nucleotide sequences of the VGAM1606 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1606 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1606 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1606 are further described hereinbelow with reference to Table 1.

[54660] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1606 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1606 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54661] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1606 gene, herein designated VGAM is inhibition of expression of VGAM1606 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1606 correlate with, and may be deduced from, the identity of the target genes which VGAM1606 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54662] ATPase, Class VI, Type 11B (ATP11B, Accession XM\_087254) is a VGAM1606 host target gene. ATP11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP11B BINDING SITE, designated SEQ ID:39149, to the nucleotide sequence of VGAM1606 RNA, herein designated VGAM RNA, also designated SEQ ID:4317.

[54663] A function of VGAM1606 is therefore inhibition of ATPase, Class VI, Type 11B (ATP11B, Accession XM\_087254), a gene which is phosphorylated in their intermediate state, drives uphill transport of ions across membranes. Accordingly, utilities of VGAM1606 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP11B. The function of ATP11B and its association with various diseases and clinical conditions, has

been established by previous studies, as described herein above with reference to VGAM665. Protein Tyrosine Phosphatase Type IVA, Member 2 (PTP4A2, Accession NM\_080392) is another VGAM1606 host target gene. PTP4A2 BINDING SITE1 and PTP4A2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTP4A2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTP4A2 BINDING SITE1 and PTP4A2 BINDING SITE2, designated SEQ ID:27831 and SEQ ID:9554 respectively, to the nucleotide sequence of VGAM1606 RNA, herein designated VGAM RNA, also designated SEQ ID:4317.

[54664] Another function of VGAM1606 is therefore inhibition of Protein Tyrosine Phosphatase Type IVA, Member 2 (PTP4A2, Accession NM\_080392), a gene which is a protein tyrosine phosphatase which has a C-terminal prenylation site. Accordingly, utilities of VGAM1606 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTP4A2. The function of PTP4A2 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM217.DNAM-1 (Accession NM\_006566) is another VGAM1606 host target gene. DNAM-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAM-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAM-1 BINDING SITE, designated SEQ ID:13340, to the nucleotide sequence of VGAM1606 RNA, herein designated VGAM RNA, also designated SEQ ID:4317.

[54665] Another function of VGAM1606 is therefore inhibition of DNAM-1 (Accession NM\_006566). Accordingly, utilities of VGAM1606 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAM-1. KIAA0426 (Accession NM\_014724) is another VGAM1606 host target gene. KIAA0426 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0426 BINDING SITE, designated SEQ ID:16313, to the

nucleotide sequence of VGAM1606 RNA, herein designated VGAM RNA, also designated SEQ ID:4317.

[54666] Another function of VGAM1606 is therefore inhibition of KIAA0426 (Accession NM\_014724). Accordingly, utilities of VGAM1606 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0426. KIAA1025 (Accession XM\_034056) is another VGAM1606 host target gene. KIAA1025 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1025 BINDING SITE, designated SEQ ID:31996, to the nucleotide sequence of VGAM1606 RNA, herein designated VGAM RNA, also designated SEQ ID:4317.

[54667] Another function of VGAM1606 is therefore inhibition of KIAA1025 (Accession XM\_034056). Accordingly, utilities of VGAM1606 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1025. KIAA1078 (Accession XM\_036589) is another VGAM1606 host target gene. KIAA1078 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1078 BINDING SITE, designated SEQ ID:32471, to the nucleotide sequence of VGAM1606 RNA, herein designated VGAM RNA, also designated SEQ ID:4317.

[54668] Another function of VGAM1606 is therefore inhibition of KIAA1078 (Accession XM\_036589). Accordingly, utilities of VGAM1606 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1078. LOC147353 (Accession XM\_097227) is another VGAM1606 host target gene. LOC147353 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147353, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147353 BINDING SITE, designated SEQ ID:40836, to the nucleotide sequence of VGAM1606 RNA, herein designated VGAM RNA, also designated SEQ ID:4317.

[54669] Another function of VGAM1606 is therefore inhibition of LOC147353 (Accession XM\_097227). Accordingly, utilities

of VGAM1606 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147353. LOC91179 (Accession XM\_036731) is another VGAM1606 host target gene. LOC91179 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91179 BINDING SITE, designated SEQ ID:32493, to the nucleotide sequence of VGAM1606 RNA, herein designated VGAM RNA, also designated SEQ ID:4317.

[54670] Another function of VGAM1606 is therefore inhibition of LOC91179 (Accession XM\_036731). Accordingly, utilities of VGAM1606 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91179. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1607 (VGAM1607) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54671] VGAM1607 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1607 was detected is described hereinabove with reference to Figs. 1–8.

[54672] VGAM1607 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Taura Syndrome Virus. VGAM1607 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54673] VGAM1607 gene encodes a VGAM1607 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1607 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1607 precursor RNA is designated SEQ ID:1593, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1593 is located at position 567 relative to the genome of Taura Syndrome Virus.

[54674] VGAM1607 precursor RNA folds onto itself, forming VGAM1607 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the



art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54675] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1607 folded precursor RNA into VGAM1607 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 89%) nucleotide sequence of VGAM1607 RNA is designated SEQ ID:4318, and is provided hereinbelow with reference to the sequence listing part.

[54676] VGAM1607 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1607 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1607 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[54677] VGAM1607 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1607 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1607 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1607 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1607 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54678] The complementary binding of VGAM1607 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1607 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1607 host target RNA into VGAM1607 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54679] It is appreciated that VGAM1607 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1607 host target genes. The mRNA of each one of this plurality of VGAM1607 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1607 RNA, herein designated VGAM RNA, and which when bound by VGAM1607 RNA causes inhibition of translation of respective one or more VGAM1607 host target proteins.

[54680] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1607 gene, herein designated VGAM GENE, on one or more VGAM1607 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54681] It is yet further appreciated that a function of VGAM1607 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1607 include diagnosis, prevention and treatment of viral infection by Taura Syndrome Virus. Specific functions, and accordingly utilities, of VGAM1607 correlate with, and may be deduced from, the identity of the host target genes which VGAM1607 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54682] Nucleotide sequences of the VGAM1607 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1607 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1607 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1607 are further  
described hereinbelow with reference to Table 1.

[54683] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1607 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1607 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[54684] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1607 gene, herein designated VGAM is  
inhibition of expression of VGAM1607 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1607 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1607  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[54685] DKFZp761G0313 (Accession XM\_038026) is a VGAM1607  
host target gene. DKFZp761G0313 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761G0313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761G0313 BINDING SITE, designated SEQ ID:32740, to the nucleotide sequence of VGAM1607 RNA, herein designated VGAM RNA, also designated SEQ ID:4318.

[54686] A function of VGAM1607 is therefore inhibition of DKFZp761G0313 (Accession XM\_038026). Accordingly, utilities of VGAM1607 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761G0313. HML2 (Accession NM\_006344) is another VGAM1607 host target gene. HML2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HML2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HML2 BINDING SITE, designated SEQ ID:13040, to the nucleotide sequence of VGAM1607 RNA, herein designated VGAM RNA, also designated SEQ ID:4318.

[54687] Another function of VGAM1607 is therefore inhibition of

HML2 (Accession NM\_006344). Accordingly, utilities of VGAM1607 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HML2. LOC139248 (Accession XM\_066582) is another VGAM1607 host target gene. LOC139248 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC139248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139248 BINDING SITE, designated SEQ ID:37336, to the nucleotide sequence of VGAM1607 RNA, herein designated VGAM RNA, also designated SEQ ID:4318.

[54688] Another function of VGAM1607 is therefore inhibition of LOC139248 (Accession XM\_066582). Accordingly, utilities of VGAM1607 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139248. LOC196746 (Accession XM\_113595) is another VGAM1607 host target gene. LOC196746 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196746, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC196746 BINDING SITE, designated SEQ ID:42290, to the nucleotide sequence of VGAM1607 RNA, herein designated VGAM RNA, also designated SEQ ID:4318.

[54689] Another function of VGAM1607 is therefore inhibition of LOC196746 (Accession XM\_113595). Accordingly, utilities of VGAM1607 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196746. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1608 (VGAM1608) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54690] VGAM1608 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1608 was detected is described hereinabove with reference to Figs. 1–8.

[54691] VGAM1608 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Taura Syndrome Virus. VGAM1608 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[54692] VGAM1608 gene encodes a VGAM1608 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1608 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1608 precursor RNA is designated SEQ ID:1594, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1594 is located at position 3052 relative to the genome of Taura Syndrome Virus.

[54693] VGAM1608 precursor RNA folds onto itself, forming VGAM1608 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54694] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1608 folded precursor RNA into VGAM1608 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1608 RNA is designated SEQ ID:4319, and is provided hereinbelow with reference to the sequence listing part.

[54695] VGAM1608 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1608 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1608 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54696] VGAM1608 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1608 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1608 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1608 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1608 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54697] The complementary binding of VGAM1608 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1608 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1608 host target RNA into VGAM1608 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54698] It is appreciated that VGAM1608 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1608 host target genes. The mRNA of each one of this plurality of VGAM1608 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1608 RNA, herein designated VGAM RNA, and which when bound by VGAM1608 RNA causes inhibition of translation of respective one or more VGAM1608 host target proteins.

[54699] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1608 gene, herein designated VGAM GENE, on one or more VGAM1608 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54700] It is yet further appreciated that a function of VGAM1608 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1608 include diagnosis, prevention and treatment of viral infection by Taura Syndrome Virus. Specific functions, and accordingly utilities, of VGAM1608 correlate with, and may be deduced from, the identity of the host target genes which VGAM1608 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54701] Nucleotide sequences of the VGAM1608 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1608 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1608 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1608 are further described hereinbelow with reference to Table 1.

[54702] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1608 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1608 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54703] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1608 gene, herein designated VGAM is inhibition of expression of VGAM1608 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1608 correlate with, and may be deduced from, the identity of the target genes which VGAM1608 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54704] LFG (Accession XM\_084780) is a VGAM1608 host target gene. LFG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LFG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LFG BINDING SITE, designated SEQ ID:37689, to the nucleotide sequence of VGAM1608 RNA, herein designated VGAM RNA, also designated SEQ ID:4319.

[54705] A function of VGAM1608 is therefore inhibition of LFG

(Accession XM\_084780). Accordingly, utilities of VGAM1608 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LFG. Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 4 (MLLT4, Accession XM\_051832) is another VGAM1608 host target gene. MLLT4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MLLT4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT4 BINDING SITE, designated SEQ ID:35888, to the nucleotide sequence of VGAM1608 RNA, herein designated VGAM RNA, also designated SEQ ID:4319.

[54706] Another function of VGAM1608 is therefore inhibition of Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 4 (MLLT4, Accession XM\_051832), a gene which may act as an intracellular signaling component. Accordingly, utilities of VGAM1608 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT4. The function of MLLT4 has been established by previous studies.

Most acute leukemias in infancy and at least 5% of acute lymphoblastic leukemias and acute myeloid leukemias of older children and adults show abnormalities of chromosome band 11q23. In these cases, translocation results in fusion of a gene at 11q23, variously called ALL1, MLL, and the human homolog of *Drosophila* 'trithorax' (OMIM Ref. No. 159555), with part of a gene on chromosome 4 (OMIM Ref. No. 159557), chromosome 9 (OMIM Ref. No. 159558), or chromosome 19 (OMIM Ref. No. 159556). Prasad et al. (1993) described the cloning and characterization of the 'partner gene' involved in a fourth common translocation involving 11q23, t(6;11)(q27;q23). The gene, designated AF6 by them, was found to be expressed in a variety of cell types and to encode a protein of 1,612 amino acids. The protein contains short stretches rich in proline, charged amino acids, serines, or glutamines. In addition, the AF6 protein contains the GLGF motif shared with several proteins of vertebrates and invertebrates thought to be involved in signal transduction at special cell-cell junctions. Using rapid amplification of cDNA ends (RACE) by PCR, Saha et al. (1995) confirmed the breakpoint in AF6 and identified a cDNA clone that was used as a probe to screen a chromosome 6 cosmid library. By flu-



orescence in situ hybridization, the single clone that was isolated was found to map distal to the critically deleted region associated with ovarian malignancies (OMIM Ref. No. 167000). AF6 is therefore distinct from and lies telomeric to that region. This gene is also symbolized MLLT4.

[54707] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54708] Prasad, R.; Gu, Y.; Alder, H.; Nakamura, T.; Canaani, O.; Saito, H.; Huebner, K.; Gale, R. P.; Nowell, P. C.; Kuriyama, K.; Miyazaki, Y.; Croce, C. M.; Canaani, E. : Cloning of the ALL-1 fusion partner, the AF-6 gene, involved in acute myeloid leukemias with the t(6;11) chromosome translocation. Cancer Res. 53: 5624-5628, 1993. ; and

[54709] Saha, V.; Lillington, D. M.; Shelling, A. N.; Chaplin, T.; Yaspo, M.-L.; Ganesan, T. S.; Young, B. D. : AF6 gene on chromosome band 6q27 maps distal to the minimal region of deletion in.

[54710] Further studies establishing the function and utilities of MLLT4 are found in John Hopkins OMIM database record ID 159559, and in cited publications numbered 1846-1847 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Vang-like 2 (van gogh, Drosophila) (VANGL2, Accession XM\_049695) is another VGAM1608 host target gene. VANGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VANGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VANGL2 BINDING SITE, designated SEQ ID:35484, to the nucleotide sequence of VGAM1608 RNA, herein designated VGAM RNA, also designated SEQ ID:4319.

[54711] Another function of VGAM1608 is therefore inhibition of Vang-like 2 (van gogh, Drosophila) (VANGL2, Accession XM\_049695), a gene which may take part in defining the lateral boundary of floorplate differentiation. Accordingly, utilities of VGAM1608 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VANGL2. The function of VANGL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM111.NY-REN-25 (Accession XM\_027116) is another VGAM1608 host target gene. NY-REN-25 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by NY-REN-25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-25 BINDING SITE, designated SEQ ID:30420, to the nucleotide sequence of VGAM1608 RNA, herein designated VGAM RNA, also designated SEQ ID:4319.

[54712] Another function of VGAM1608 is therefore inhibition of NY-REN-25 (Accession XM\_027116). Accordingly, utilities of VGAM1608 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-25. LOC219333 (Accession XM\_167944) is another VGAM1608 host target gene. LOC219333 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219333 BINDING SITE, designated SEQ ID:44933, to the nucleotide sequence of VGAM1608 RNA, herein designated VGAM RNA, also designated SEQ ID:4319.

[54713] Another function of VGAM1608 is therefore inhibition of

LOC219333 (Accession XM\_167944). Accordingly, utilities of VGAM1608 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219333. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1609 (VGAM1609) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54714] VGAM1609 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1609 was detected is described hereinabove with reference to Figs. 1-8.

[54715] VGAM1609 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1609 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54716] VGAM1609 gene encodes a VGAM1609 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1609 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1609 precursor RNA is designated SEQ ID:1595, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1595 is located at position 8708 relative to the genome of Chimpanzee Cytomegalovirus.

- [54717] VGAM1609 precursor RNA folds onto itself, forming VGAM1609 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54718] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1609 folded precursor RNA into VGAM1609 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide se-

quence of VGAM1609 RNA is designated SEQ ID:4320, and is provided hereinbelow with reference to the sequence listing part.

[54719] VGAM1609 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1609 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1609 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54720] VGAM1609 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1609 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1609 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1609 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1609 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[54721] The complementary binding of VGAM1609 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1609 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1609 host target RNA into VGAM1609 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54722] It is appreciated that VGAM1609 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1609 host target genes. The mRNA of each one of this plurality of VGAM1609 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1609 RNA, herein designated VGAM RNA, and which when bound by VGAM1609 RNA causes inhibition of translation of respective one or more VGAM1609 host target proteins.

[54723] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1609 gene, herein designated VGAM GENE, on one or more VGAM1609 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54724] It is yet further appreciated that a function of VGAM1609



is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1609 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1609 correlate with, and may be deduced from, the identity of the host target genes which VGAM1609 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54725] Nucleotide sequences of the VGAM1609 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1609 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1609 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1609 are further described hereinbelow with reference to Table 1.

[54726] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1609 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1609 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54727] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1609 gene, herein designated VGAM is inhibition of expression of VGAM1609 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1609 correlate with, and may be deduced from, the identity of the target genes which VGAM1609 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54728] C-myc Binding Protein (MYCBP, Accession NM\_012333) is a VGAM1609 host target gene. MYCBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYCBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYCBP BINDING SITE, designated SEQ ID:14722, to the nucleotide sequence of VGAM1609 RNA, herein designated VGAM RNA, also designated SEQ ID:4320.

[54729] A function of VGAM1609 is therefore inhibition of C-myc Binding Protein (MYCBP, Accession NM\_012333), a gene which binds c-Myc stimulating the activation of E-box-dependent transcription. Accordingly, utilities of VGAM1609 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MYCBP. The function of MYCBP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM435. Palmitoyl-protein Thioesterase 2 (PPT2, Accession NM\_138934) is another VGAM1609 host target gene. PPT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPT2 BINDING SITE, designated SEQ ID:29060, to the nucleotide sequence of VGAM1609 RNA, herein designated VGAM RNA, also designated SEQ ID:4320.

[54730] Another function of VGAM1609 is therefore inhibition of Palmitoyl-protein Thioesterase 2 (PPT2, Accession NM\_138934), a gene which is a palmitoyl-protein thioesterase 2 which possesses a different substrate specificity than PPT1. Accordingly, utilities of VGAM1609 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPT2. The function of PPT2 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM120. Protein Tyrosine Phosphatase, Receptor Type, A (PTPRA, Accession NM\_002836) is another VGAM1609 host target gene. PTPRA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTPRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRA BINDING SITE, designated SEQ ID:8713, to the nucleotide sequence of VGAM1609 RNA, herein designated VGAM RNA, also designated SEQ ID:4320.

[54731] Another function of VGAM1609 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, A (PTPRA, Accession NM\_002836), a gene which is the human homolog of the murine PTPase. Accordingly, utilities of VGAM1609 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRA. The function of PTPRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1205.FLJ12681 (Accession NM\_022773) is another VGAM1609 host target gene. FLJ12681 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12681 BINDING SITE, designated SEQ ID:23034, to the nucleotide sequence of VGAM1609 RNA, herein designated VGAM RNA, also designated SEQ ID:4320.

[54732] Another function of VGAM1609 is therefore inhibition of FLJ12681 (Accession NM\_022773). Accordingly, utilities of VGAM1609 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12681. KIAA0284 (Accession XM\_032235) is another VGAM1609 host target gene. KIAA0284 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0284, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0284 BINDING SITE, designated SEQ ID:31615, to the nucleotide sequence of VGAM1609 RNA, herein designated VGAM RNA, also designated SEQ ID:4320.

[54733] Another function of VGAM1609 is therefore inhibition of

KIAA0284 (Accession XM\_032235). Accordingly, utilities of VGAM1609 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0284. LOC222161 (Accession XM\_166596) is another VGAM1609 host target gene. LOC222161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222161 BINDING SITE, designated SEQ ID:44581, to the nucleotide sequence of VGAM1609 RNA, herein designated VGAM RNA, also designated SEQ ID:4320.

[54734] Another function of VGAM1609 is therefore inhibition of LOC222161 (Accession XM\_166596). Accordingly, utilities of VGAM1609 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222161. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1610 (VGAM1610) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[54735] VGAM1610 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1610 was detected is described hereinabove with reference to Figs. 1–8.

[54736] VGAM1610 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1610 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54737] VGAM1610 gene encodes a VGAM1610 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1610 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1610 precursor RNA is designated SEQ ID:1596, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1596 is located at position 5615 relative to the genome of Chimpanzee Cytomegalovirus.

[54738] VGAM1610 precursor RNA folds onto itself, forming VGAM1610 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54739] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1610 folded precursor RNA into VGAM1610 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1610 RNA is designated SEQ ID:4321, and is provided hereinbelow with reference to the sequence listing part.

[54740] VGAM1610 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1610 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1610 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-



ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[54741] VGAM1610 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1610 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1610 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1610 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1610 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[54742] The complementary binding of VGAM1610 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1610 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1610 host target RNA into VGAM1610 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54743] It is appreciated that VGAM1610 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1610 host target genes. The mRNA of each one of this plurality of VGAM1610 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1610 RNA, herein designated VGAM RNA, and which when bound by VGAM1610 RNA causes inhibition of translation of respective one or more VGAM1610 host target proteins.

[54744] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1610 gene, herein designated VGAM GENE, on one

or more VGAM1610 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54745] It is yet further appreciated that a function of VGAM1610 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1610 correlate with, and may be deduced from, the identity of the host target genes which VGAM1610 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54746] Nucleotide sequences of the VGAM1610 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1610 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1610 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1610 are further described hereinbelow with reference to Table 1.

[54747] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1610 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1610 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54748] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1610 gene, herein designated VGAM is inhibition of expression of VGAM1610 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1610 correlate with, and may be deduced from, the identity of the target genes which VGAM1610 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54749] Cytochrome P450, Subfamily I (aromatic compound-in-

ducible), Polypeptide 2 (CYP1A2, Accession XM\_044660) is a VGAM1610 host target gene. CYP1A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP1A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP1A2 BINDING SITE, designated SEQ ID:34254, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54750] A function of VGAM1610 is therefore inhibition of Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 2 (CYP1A2, Accession XM\_044660), a gene which intervenes in an NADPH-dependent electron transport pathway. Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP1A2. The function of CYP1A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Poliovirus Receptor (PVR, Accession NM\_006505) is another VGAM1610 host target gene. PVR BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PVR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PVR BINDING SITE, designated SEQ ID:13252, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54751] Another function of VGAM1610 is therefore inhibition of Poliovirus Receptor (PVR, Accession NM\_006505), a gene which is a poliovirus receptor. Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PVR. The function of PVR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1411. Tumor Necrosis Factor Receptor Superfamily, Member 8 (TNFRSF8, Accession NM\_001243) is another VGAM1610 host target gene. TNFRSF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF8

BINDING SITE, designated SEQ ID:6909, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54752] Another function of VGAM1610 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 8 (TNFRSF8, Accession NM\_001243), a gene which regulates gene expression through activation of nf-kappab. Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF8. The function of TNFRSF8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM154. Hyaluronan Binding Protein 4 (HABP4, Accession XM\_047263) is another VGAM1610 host target gene. HABP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HABP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HABP4 BINDING SITE, designated SEQ ID:34924, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54753] Another function of VGAM1610 is therefore inhibition of Hyaluronan Binding Protein 4 (HABP4, Accession XM\_047263). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HABP4. KIAA1280 (Accession XM\_045766) is another VGAM1610 host target gene. KIAA1280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1280 BINDING SITE, designated SEQ ID:34549, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54754] Another function of VGAM1610 is therefore inhibition of KIAA1280 (Accession XM\_045766). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1280. Kelch-like 6 (Drosophila) (KLHL6, Accession NM\_130446) is another VGAM1610 host target gene. KLHL6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL6,



corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL6 BINDING SITE, designated SEQ ID:28208, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54755] Another function of VGAM1610 is therefore inhibition of Kelch-like 6 (*Drosophila*) (KLHL6, Accession NM\_130446). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL6. OS4 (Accession NM\_005730) is another VGAM1610 host target gene. OS4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OS4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OS4 BINDING SITE, designated SEQ ID:12286, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54756] Another function of VGAM1610 is therefore inhibition of OS4 (Accession NM\_005730). Accordingly, utilities of

VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OS4. PME-1 (Accession NM\_016147) is another VGAM1610 host target gene. PME-1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PME-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PME-1 BINDING SITE, designated SEQ ID:18230, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54757] Another function of VGAM1610 is therefore inhibition of PME-1 (Accession NM\_016147). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PME-1. SARM (Accession NM\_015077) is another VGAM1610 host target gene. SARM BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SARM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SARM BINDING SITE, designated SEQ

ID:17451, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54758] Another function of VGAM1610 is therefore inhibition of SARM (Accession NM\_015077). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SARM. LOC124930 (Accession XM\_058867) is another VGAM1610 host target gene. LOC124930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124930 BINDING SITE, designated SEQ ID:36765, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54759] Another function of VGAM1610 is therefore inhibition of LOC124930 (Accession XM\_058867). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124930. LOC149276 (Accession XM\_097621) is another VGAM1610 host target gene. LOC149276 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149276 BINDING SITE, designated SEQ ID:40974, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54760] Another function of VGAM1610 is therefore inhibition of LOC149276 (Accession XM\_097621). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149276. LOC157848 (Accession XM\_088405) is another VGAM1610 host target gene. LOC157848 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157848 BINDING SITE, designated SEQ ID:39671, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54761] Another function of VGAM1610 is therefore inhibition of

LOC157848 (Accession XM\_088405). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157848. LOC158292 (Accession XM\_098914) is another VGAM1610 host target gene. LOC158292 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158292 BINDING SITE, designated SEQ ID:41930, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54762] Another function of VGAM1610 is therefore inhibition of LOC158292 (Accession XM\_098914). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158292. LOC253893 (Accession XM\_171188) is another VGAM1610 host target gene. LOC253893 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC253893 BINDING SITE, designated SEQ ID:45970, to the nucleotide sequence of VGAM1610 RNA, herein designated VGAM RNA, also designated SEQ ID:4321.

[54763] Another function of VGAM1610 is therefore inhibition of LOC253893 (Accession XM\_171188). Accordingly, utilities of VGAM1610 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253893. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1611 (VGAM1611) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54764] VGAM1611 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1611 was detected is described hereinabove with reference to Figs. 1–8.

[54765] VGAM1611 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1611 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[54766] VGAM1611 gene encodes a VGAM1611 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1611 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1611 precursor RNA is designated SEQ ID:1597, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1597 is located at position 10114 relative to the genome of Chimpanzee Cytomegalovirus.

[54767] VGAM1611 precursor RNA folds onto itself, forming VGAM1611 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54768] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1611 folded precursor RNA into VGAM1611 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1611 RNA is designated SEQ ID:4322, and is provided hereinbelow with reference to the sequence listing part.

[54769] VGAM1611 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1611 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1611 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54770] VGAM1611 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1611 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1611 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-



quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1611 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1611 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54771] The complementary binding of VGAM1611 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1611 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1611 host target RNA into VGAM1611 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54772] It is appreciated that VGAM1611 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1611 host target genes. The mRNA of each one of this plurality of VGAM1611 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1611 RNA, herein designated VGAM RNA, and which when bound by VGAM1611 RNA causes inhibition of translation of respective one or more VGAM1611 host target proteins.

[54773] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1611 gene, herein designated VGAM GENE, on one or more VGAM1611 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54774] It is yet further appreciated that a function of VGAM1611 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1611 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cy-tomegalovirus. Specific functions, and accordingly utilities, of VGAM1611 correlate with, and may be deduced from, the identity of the host target genes which VGAM1611 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54775] Nucleotide sequences of the VGAM1611 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1611 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1611 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1611 are further described hereinbelow with reference to Table 1.

[54776] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1611 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1611 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54777] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1611 gene, herein designated VGAM is inhibition of expression of VGAM1611 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1611 correlate with, and may be deduced from, the identity of the target genes which VGAM1611 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54778] Leukemia Inhibitory Factor Receptor (LIFR, Accession NM\_002310) is a VGAM1611 host target gene. LIFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIFR BINDING SITE, designated SEQ ID:8102, to the nucleotide sequence of VGAM1611 RNA, herein designated VGAM RNA, also designated SEQ ID:4322.

[54779] A function of VGAM1611 is therefore inhibition of Leukemia Inhibitory Factor Receptor (LIFR, Accession NM\_002310). Accordingly, utilities of VGAM1611 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIFR. BTB (POZ) Domain Containing 3 (BTBD3, Accession NM\_014962) is another VGAM1611 host target gene. BTBD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTBD3 BINDING SITE, designated SEQ ID:17338, to the nucleotide sequence of VGAM1611 RNA, herein designated VGAM RNA, also designated SEQ ID:4322.

[54780] Another function of VGAM1611 is therefore inhibition of BTB (POZ) Domain Containing 3 (BTBD3, Accession NM\_014962). Accordingly, utilities of VGAM1611 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTBD3. LOC149351 (Accession XM\_086503) is another VGAM1611 host target gene. LOC149351 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by LOC149351, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149351 BINDING SITE, designated SEQ ID:38716, to the nucleotide sequence of VGAM1611 RNA, herein designated VGAM RNA, also designated SEQ ID:4322.

[54781] Another function of VGAM1611 is therefore inhibition of LOC149351 (Accession XM\_086503). Accordingly, utilities of VGAM1611 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149351. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1612 (VGAM1612) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54782] VGAM1612 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1612 was detected is described hereinabove with reference to Figs. 1-8.

[54783] VGAM1612 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1612 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54784] VGAM1612 gene encodes a VGAM1612 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1612 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1612 precursor RNA is designated SEQ ID:1598, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1598 is located at position 1800 relative to the genome of Chimpanzee Cytomegalovirus.

[54785] VGAM1612 precursor RNA folds onto itself, forming VGAM1612 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54786] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1612 folded precursor RNA into VGAM1612 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1612 RNA is designated SEQ ID:4323, and is provided hereinbelow with reference to the sequence listing part.

[54787] VGAM1612 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1612 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1612 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54788] VGAM1612 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1612 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM1612 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1612 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1612 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54789] The complementary binding of VGAM1612 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1612 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1612

host target RNA into VGAM1612 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54790] It is appreciated that VGAM1612 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1612 host target genes. The mRNA of each one of this plurality of VGAM1612 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1612 RNA, herein designated VGAM RNA, and which when bound by VGAM1612 RNA causes inhibition of translation of respective one or more VGAM1612 host target proteins.

[54791] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1612 gene, herein designated VGAM GENE, on one or more VGAM1612 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54792] It is yet further appreciated that a function of VGAM1612 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1612 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1612 correlate with, and may be deduced from, the identity of the host target genes which VGAM1612 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54793] Nucleotide sequences of the VGAM1612 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1612 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1612 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1612 are further

described hereinbelow with reference to Table 1.

[54794] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1612 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1612 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54795] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1612 gene, herein designated VGAM is inhibition of expression of VGAM1612 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1612 correlate with, and may be deduced from, the identity of the target genes which VGAM1612 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54796] KIAA1679 (Accession XM\_046570) is a VGAM1612 host target gene. KIAA1679 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1679, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1679 BINDING SITE,

designated SEQ ID:34750, to the nucleotide sequence of VGAM1612 RNA, herein designated VGAM RNA, also designated SEQ ID:4323.

[54797] A function of VGAM1612 is therefore inhibition of KIAA1679 (Accession XM\_046570). Accordingly, utilities of VGAM1612 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1679. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1613 (VGAM1613) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54798] VGAM1613 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1613 was detected is described hereinabove with reference to Figs. 1-8.

[54799] VGAM1613 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1613 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54800] VGAM1613 gene encodes a VGAM1613 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1613 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1613 precursor RNA is designated SEQ ID:1599, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1599 is located at position 4267 relative to the genome of Chimpanzee Cytomegalovirus.

[54801] VGAM1613 precursor RNA folds onto itself, forming VGAM1613 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54802] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1613 folded precursor RNA into VGAM1613 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide sequence of VGAM1613 RNA is designated SEQ ID:4324, and is provided hereinbelow with reference to the sequence listing part.

[54803] VGAM1613 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1613 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1613 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54804] VGAM1613 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1613 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1613 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1613 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1613 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54805] The complementary binding of VGAM1613 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1613 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1613 host target RNA into VGAM1613 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54806] It is appreciated that VGAM1613 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1613 host target genes. The mRNA of each one of this plurality of VGAM1613 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1613 RNA, herein designated VGAM RNA, and which when bound by VGAM1613 RNA causes inhibition of translation of respective one or more VGAM1613 host target proteins.

[54807] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1613 gene, herein designated VGAM GENE, on one or more VGAM1613 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[54808] It is yet further appreciated that a function of VGAM1613 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1613 correlate with, and may be deduced from, the identity of the host target genes which VGAM1613 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54809] Nucleotide sequences of the VGAM1613 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1613 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1613 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1613 are further described hereinbelow with reference to Table 1.

[54810] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1613 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1613 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54811] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1613 gene, herein designated VGAM is inhibition of expression of VGAM1613 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1613 correlate with, and may be deduced from, the identity of the target genes which VGAM1613 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54812] Cytokine Receptor-like Factor 1 (CRLF1, Accession NM\_004750) is a VGAM1613 host target gene. CRLF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CRLF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRLF1 BINDING SITE, designated SEQ ID:11139, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54813] A function of VGAM1613 is therefore inhibition of Cy-

tokine Receptor-like Factor 1 (CRLF1, Accession NM\_004750), a gene which is similar to cytokine type 1 receptors. Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRLF1. The function of CRLF1 has been established by previous studies. Elson et al. (1998) described the identification, cloning, and expression pattern of human cytokine-like factor-1, which they designated CLF1, as well as the identification and cloning of the mouse homolog. They were identified from expressed sequence tags using amino acid sequences from conserved regions of the cytokine type I receptor family. The human and mouse CRLF1 proteins share 96% amino acid identity and significant homology with many cytokine type I receptors. The human cDNA encodes a precursor protein of 422 amino acids with a putative signal peptide of 37 amino acids. CRLF1 is a secreted protein, suggesting that it is either a soluble subunit within a cytokine receptor complex, like the soluble form of IL6R (OMIM Ref. No. 147880) or a subunit of a multimeric cytokine, e.g., IL12B (OMIM Ref. No. 161561). The highest levels of CRLF1 mRNA were observed in lymph node, spleen, thymus, appendix, placenta, stomach, and fetal lung, with

constitutive expression of CRLF1 mRNA detected in a human kidney fibroblast cell line. In fibroblast primary cell cultures, CRLF1 mRNA was upregulated by TNF- $\alpha$  (OMIM Ref. No. 191160), interleukin-6 (OMIM Ref. No. 147620), and gamma-interferon (OMIM Ref. No. 147570). Western blot analysis of recombinant forms of CRLF1 showed that the protein has the tendency to form covalently linked dimers and tetramers. These results suggested that CRLF1 is a novel soluble cytokine receptor subunit or part of a novel cytokine complex, possibly playing a regulatory role in the immune system and during fetal development Alexander et al. (1999) found that, although in situ hybridization showed Nr6 expression at multiple sites in the developing embryo, mice lacking Nr6 did not display obvious abnormalities and were born in the expected numbers. Neonatal Nr6  $-/-$  mice failed to suckle, however, and died within 24 hours of birth, suggesting that Nr6 is necessary for the recognition of processing pheromonal signals or for the mechanics of suckling itself. In addition, Nr6  $-/-$  mice had reduced numbers of hemopoietic progenitor cells, suggesting a potential role in the regulation of primitive hemopoiesis

[54814] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [54815] Elson, G. C. A.; Graber, P.; Losberger, C.; Herren, S.; Gretener, D.; Menoud, L. N.; Wells, T. N. C.; Kosco-Vilbois, M. H.; Gauchat, J.-F. : Cytokine-like factor-1, a novel soluble protein, shares homology with members of the cytokine type I receptor family. *J. Immun.* 161: 1371-1379, 1998. ; and
- [54816] Alexander, W. S.; Rakar, S.; Robb, L.; Farley, A.; Willson, T. A.; Zhang, J.-G.; Hartley, L.; Kikuchi, Y.; Kojima, T.; Nomura, H.; Hasegawa, M.; Maeda, M.; Fabri, L.; Jachno, K.; Nash, A.
- [54817] Further studies establishing the function and utilities of CRLF1 are found in John Hopkins OMIM database record ID 604237, and in cited publications numbered 5176-5177 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Enolase 2, (gamma, neuronal) (ENO2, Accession NM\_001975) is another VGAM1613 host target gene. ENO2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ENO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ENO2 BINDING SITE, designated SEQ ID:7705, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54818] Another function of VGAM1613 is therefore inhibition of Enolase 2, (gamma, neuronal) (ENO2, Accession NM\_001975), a gene which converts 2-phospho-D-glycerate to phosphoenolpyruvate in glycolysis. Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENO2. The function of ENO2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1151. Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 2 (KCNS2, Accession XM\_043106) is another VGAM1613 host target gene. KCNS2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNS2 BINDING SITE, designated SEQ

ID:33900, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54819] Another function of VGAM1613 is therefore inhibition of Potassium Voltage-gated Channel, Delayed-rectifier, Sub-family S, Member 2 (KCNS2, Accession XM\_043106), a gene which mediates the voltage-dependent potassium ion permeability of excitable membranes. Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNS2. The function of KCNS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM419. Matrix Metalloproteinase 14 (membrane-inserted) (MMP14, Accession NM\_004995) is another VGAM1613 host target gene. MMP14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MMP14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP14 BINDING SITE, designated SEQ ID:11435, to the nucleotide sequence of VGAM1613 RNA, herein design-



nated VGAM RNA, also designated SEQ ID:4324.

[54820] Another function of VGAM1613 is therefore inhibition of Matrix Metalloproteinase 14 (membrane-inserted) (MMP14, Accession NM\_004995). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP14. FLJ14753 (Accession NM\_032558) is another VGAM1613 host target gene. FLJ14753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14753 BINDING SITE, designated SEQ ID:26285, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54821] Another function of VGAM1613 is therefore inhibition of FLJ14753 (Accession NM\_032558). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14753. KIAA0229 (Accession XM\_166478) is another VGAM1613 host target gene. KIAA0229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0229 BINDING SITE, designated SEQ ID:44397, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54822] Another function of VGAM1613 is therefore inhibition of KIAA0229 (Accession XM\_166478). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0229. KIAA0537 (Accession NM\_014840) is another VGAM1613 host target gene. KIAA0537 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0537, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0537 BINDING SITE, designated SEQ ID:16865, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54823] Another function of VGAM1613 is therefore inhibition of KIAA0537 (Accession NM\_014840). Accordingly, utilities

of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0537. MGC20235 (Accession NM\_145041) is another VGAM1613 host target gene. MGC20235 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC20235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20235 BINDING SITE, designated SEQ ID:29664, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54824] Another function of VGAM1613 is therefore inhibition of MGC20235 (Accession NM\_145041). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20235. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4G (SEMA4G, Accession XM\_170638) is another VGAM1613 host target gene. SEMA4G BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEMA4G, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4G BINDING SITE, designated SEQ ID:45410, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54825] Another function of VGAM1613 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4G (SEMA4G, Accession XM\_170638). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4G. Vesicular Inhibitory Amino Acid Transporter (VIAAT, Accession NM\_080552) is another VGAM1613 host target gene. VIAAT BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by VIAAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VIAAT BINDING SITE, designated SEQ ID:27884, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54826] Another function of VGAM1613 is therefore inhibition of

Vesicular Inhibitory Amino Acid Transporter (VIAAT, Accession NM\_080552). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIAAT. LOC145989 (Accession XM\_004815) is another VGAM1613 host target gene. LOC145989 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145989 BINDING SITE, designated SEQ ID:29948, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54827] Another function of VGAM1613 is therefore inhibition of LOC145989 (Accession XM\_004815). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145989. LOC148946 (Accession XM\_097557) is another VGAM1613 host target gene. LOC148946 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC148946, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148946 BINDING SITE, designated SEQ ID:40938, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54828] Another function of VGAM1613 is therefore inhibition of LOC148946 (Accession XM\_097557). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148946. LOC151127 (Accession XM\_087104) is another VGAM1613 host target gene. LOC151127 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151127 BINDING SITE, designated SEQ ID:39060, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54829] Another function of VGAM1613 is therefore inhibition of LOC151127 (Accession XM\_087104). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC151127. LOC201175 (Accession XM\_113915) is another VGAM1613 host target gene. LOC201175 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201175 BINDING SITE, designated SEQ ID:42533, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54830] Another function of VGAM1613 is therefore inhibition of LOC201175 (Accession XM\_113915). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201175. LOC220558 (Accession XM\_165930) is another VGAM1613 host target gene. LOC220558 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220558 BINDING SITE, designated SEQ ID:43804, to the nucleotide sequence of VGAM1613 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4324.

[54831] Another function of VGAM1613 is therefore inhibition of LOC220558 (Accession XM\_165930). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220558. LOC221250 (Accession XM\_166301) is another VGAM1613 host target gene. LOC221250 BINDING SITE1 and LOC221250 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC221250, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221250 BINDING SITE1 and LOC221250 BINDING SITE2, designated SEQ ID:44118 and SEQ ID:44119 respectively, to the nucleotide sequence of VGAM1613 RNA, herein designated VGAM RNA, also designated SEQ ID:4324.

[54832] Another function of VGAM1613 is therefore inhibition of LOC221250 (Accession XM\_166301). Accordingly, utilities of VGAM1613 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221250. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the



present invention, referred to here as Viral Genomic Address Messenger 1614 (VGAM1614) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54833] VGAM1614 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1614 was detected is described hereinabove with reference to Figs. 1–8.

[54834] VGAM1614 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1614 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54835] VGAM1614 gene encodes a VGAM1614 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1614 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1614 precursor RNA is designated SEQ ID:1600, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1600 is located at position 6443 relative to the

genome of Chimpanzee Cytomegalovirus.

[54836] VGAM1614 precursor RNA folds onto itself, forming VGAM1614 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54837] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1614 folded precursor RNA into VGAM1614 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1614 RNA is designated SEQ ID:4325, and is provided hereinbelow with reference to the sequence listing part.

[54838] VGAM1614 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1614 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1614 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54839] VGAM1614 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1614 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1614 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1614 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1614 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54840] The complementary binding of VGAM1614 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1614 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1614 host target RNA into VGAM1614 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54841] It is appreciated that VGAM1614 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1614 host target genes. The mRNA of each one of this plurality of VGAM1614 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1614 RNA, herein designated VGAM RNA, and which when bound by VGAM1614 RNA causes inhibition of translation of respective one or more VGAM1614 host target proteins.

[54842] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1614 gene, herein designated VGAM GENE, on one or more VGAM1614 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54843] It is yet further appreciated that a function of VGAM1614 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1614 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utili-

ties, of VGAM1614 correlate with, and may be deduced from, the identity of the host target genes which VGAM1614 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54844] Nucleotide sequences of the VGAM1614 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1614 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1614 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1614 are further described hereinbelow with reference to Table 1.

[54845] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1614 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1614 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54846] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1614 gene, herein designated VGAM is inhibition of expression of VGAM1614 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1614 correlate with, and may be deduced

from, the identity of the target genes which VGAM1614 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54847] ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM\_036933) is a VGAM1614 host target gene. ATP8B2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ATP8B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8B2 BINDING SITE, designated SEQ ID:32514, to the nucleotide sequence of VGAM1614 RNA, herein designated VGAM RNA, also designated SEQ ID:4325.

[54848] A function of VGAM1614 is therefore inhibition of ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM\_036933). Accordingly, utilities of VGAM1614 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8B2. PRV1 (Accession XM\_056490) is another VGAM1614 host target gene. PRV1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of PRV1 BINDING SITE, designated SEQ ID:36398, to the nucleotide sequence of VGAM1614 RNA, herein designated VGAM RNA, also designated SEQ ID:4325.

[54849] Another function of VGAM1614 is therefore inhibition of PRV1 (Accession XM\_056490), a gene which may function as a hematopoietic receptor. Accordingly, utilities of VGAM1614 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRV1. The function of PRV1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM778.C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM\_031910) is another VGAM1614 host target gene. C1QTNF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1QTNF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QTNF6 BINDING SITE, designated SEQ ID:25657, to the nucleotide sequence of VGAM1614 RNA, herein designated VGAM RNA, also designated SEQ ID:4325.



[54850] Another function of VGAM1614 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM\_031910). Accordingly, utilities of VGAM1614 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF6. FLJ10726 (Accession NM\_018195) is another VGAM1614 host target gene. FLJ10726 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10726, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10726 BINDING SITE, designated SEQ ID:20057, to the nucleotide sequence of VGAM1614 RNA, herein designated VGAM RNA, also designated SEQ ID:4325.

[54851] Another function of VGAM1614 is therefore inhibition of FLJ10726 (Accession NM\_018195). Accordingly, utilities of VGAM1614 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10726. LOC145854 (Accession XM\_085259) is another VGAM1614 host target gene. LOC145854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145854, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145854 BINDING SITE, designated SEQ ID:38007, to the nucleotide sequence of VGAM1614 RNA, herein designated VGAM RNA, also designated SEQ ID:4325.

[54852] Another function of VGAM1614 is therefore inhibition of LOC145854 (Accession XM\_085259). Accordingly, utilities of VGAM1614 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145854. LOC157273 (Accession XM\_098743) is another VGAM1614 host target gene. LOC157273 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157273 BINDING SITE, designated SEQ ID:41783, to the nucleotide sequence of VGAM1614 RNA, herein designated VGAM RNA, also designated SEQ ID:4325.

[54853] Another function of VGAM1614 is therefore inhibition of LOC157273 (Accession XM\_098743). Accordingly, utilities of VGAM1614 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC157273. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1615 (VGAM1615) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54854] VGAM1615 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1615 was detected is described hereinabove with reference to Figs. 1–8.

[54855] VGAM1615 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1615 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54856] VGAM1615 gene encodes a VGAM1615 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1615 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1615 precursor RNA is desig-

nated SEQ ID:1601, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1601 is located at position 1492 relative to the genome of Chimpanzee Cytomegalovirus.

- [54857] VGAM1615 precursor RNA folds onto itself, forming VGAM1615 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [54858] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1615 folded precursor RNA into VGAM1615 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1615 RNA is designated SEQ ID:4326, and is provided hereinbelow with reference to the sequence

listing part.

[54859] VGAM1615 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1615 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1615 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54860] VGAM1615 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1615 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1615 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1615 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1615 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54861] The complementary binding of VGAM1615 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1615 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1615 host target RNA into VGAM1615 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54862] It is appreciated that VGAM1615 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1615 host target genes. The mRNA of each one of this plurality of VGAM1615 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1615 RNA, herein designated VGAM

RNA, and which when bound by VGAM1615 RNA causes inhibition of translation of respective one or more VGAM1615 host target proteins.

[54863] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1615 gene, herein designated VGAM GENE, on one or more VGAM1615 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54864] It is yet further appreciated that a function of VGAM1615 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1615 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1615 correlate with, and may be deduced from, the identity of the host target genes which VGAM1615 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54865] Nucleotide sequences of the VGAM1615 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1615 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1615 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1615 are further described hereinbelow with reference to Table 1.

[54866] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1615 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1615 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54867] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1615 gene, herein designated VGAM is



inhibition of expression of VGAM1615 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1615 correlate with, and may be deduced from, the identity of the target genes which VGAM1615 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54868] Bone Morphogenetic Protein 6 (BMP6, Accession NM\_001718) is a VGAM1615 host target gene. BMP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BMP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMP6 BINDING SITE, designated SEQ ID:7453, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54869] A function of VGAM1615 is therefore inhibition of Bone Morphogenetic Protein 6 (BMP6, Accession NM\_001718), a gene which induces cartilage and bone formation. Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMP6. The function of BMP6 and its association with various diseases and clinical conditions, has

been established by previous studies, as described herein above with reference to VGAM233. Cold Shock Domain Protein A (CSDA, Accession NM\_003651) is another VGAM1615 host target gene. CSDA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CSDA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSDA BINDING SITE, designated SEQ ID:9727, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54870] Another function of VGAM1615 is therefore inhibition of Cold Shock Domain Protein A (CSDA, Accession NM\_003651), a gene which binds to the gm-csf promoter and seems to act as a repressor. Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSDA. The function of CSDA has been established by previous studies. To identify cDNAs encoding DNA-binding proteins (DBPs), Sakura et al. (1988) screened a human placenta cDNA expression library with DNA fragments containing either the human epidermal growth factor receptor

(EGFR; 131550) enhancer or the human c-erbB2 (OMIM Ref. No. 164870) promoter. They isolated cDNAs encoding DBPA and DBPB (OMIM Ref. No. 154030). The DBPA cDNAs consisted of 2 forms that differ by an internal 207-bp deletion. Northern blot analysis of HeLa cell RNA detected a major 2.5-kb DBPA transcript and a minor 2.3-kb DBPA transcript. The deduced DBPA and DBPB proteins share a central region in which 100 of 109 amino acids are identical between the 2 proteins. Kudo et al. (1995) isolated full-length human cDNAs encoding DBPA and DBPB by screening for proteins that bind to the human leukosialin (OMIM Ref. No. 182160) promoter. The deduced 342-amino acid DBPA protein has a cold-shock domain and a DNA-binding domain. The authors isolated the DBPA genomic sequence and found that it contains 10 exons spanning 24 kb; exon 6, which encodes 69 amino acids, is alternatively spliced. Northern blot analysis of human tissues demonstrated highest levels of DBPA transcription in skeletal muscle and heart. Immunofluorescence detected DBPA protein expression in both the cytoplasm and nucleus of HeLa cells

[54871] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [54872] Sakura, H.; Maekawa, T.; Imamoto, F.; Yasuda, K.; Ishii, S. : Two human genes isolated by a novel method encode DNA-binding proteins containing a common region of homology. *Gene* 73: 499–507, 1988. ; and
- [54873] Kudo, S.; Mattei, M.–G.; Fukuda, M. : Characterization of the gene for dbpA, a family member of the nucleic-acid-binding proteins containing a cold-shock domain. *Europ. J. Biochem.* 231:.
- [54874] Further studies establishing the function and utilities of CSDA are found in John Hopkins OMIM database record ID 603437, and in cited publications numbered 3794–3796 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Engrailed Homolog 1 (EN1, Accession NM\_001426) is another VGAM1615 host target gene. EN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EN1 BINDING SITE, designated SEQ ID:7141, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ

ID:4326.

[54875] Another function of VGAM1615 is therefore inhibition of Engrailed Homolog 1 (EN1, Accession NM\_001426), a gene which is a member of the homeodomain family of DNA binding proteins; may regulate gene expression, morphogenesis, and differentiation;. Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EN1. The function of EN1 has been established by previous studies. In *Drosophila*, the 'engrailed' (en) gene plays an important role during development in segmentation, where it is required for the formation of posterior compartments. Expression studies have suggested that en may also function early in organizing the preblastoderm and later in neurogenesis (Logan et al., 1992). En encodes a homeodomain-containing protein that can function as a transcription factor. Logan et al. (1989) isolated the human homologs of the mouse homeo box-containing genes En1 and En2 (OMIM Ref. No. 131310), which show homology to the *Drosophila* en gene. Logan et al. (1992) isolated human and chicken genomic clones of the EN1 and EN2 genes. As in mouse, the predicted coding region of the human and chicken EN1 genes is interrupted by a

single intron. The deduced 392-amino acid human EN1 protein is 95% identical to mouse En1. By sequence analysis, the authors determined that En proteins from various species contain 5 distinct conserved subregions. The related mouse genes En1 and En2 are expressed from the 1- and approximately 5-somite stages, respectively, in a similar presumptive midhindbrain domain. However, mutations in En1 and En2 produced different phenotypes: En1 mutant mice die at birth with a large midhindbrain deletion, whereas En2 mutants survive with cerebellar defects. To determine whether these contrasting phenotypes reflect differences in temporal expression or biochemical activity of the En proteins, Hanks et al. (1995) replaced En1 coding sequences with En2 sequences in transgenic mice by gene targeting. The En2 sequences rescued all En1 mutant defects, demonstrating that the difference between En1 and En2 stems from their divergent expression patterns. Wurst et al. (1994) generated mice homozygous for a targeted deletion of the En1 homeobox. En1 mutant mice died shortly after birth and exhibited multiple developmental defects. The pattern of defects suggested a cell-autonomous role for En1 in generation and/or survival of midhindbrain precursor cells and also a non-

cell-autonomous role in signaling normal development of the limbs and possibly sternum. Loomis et al. (1996) analyzed the effects of an induced null mutation in the mouse engrailed-1 gene on ventral limb patterning. That the gene is essential was indicated by the finding that the null mice showed dorsal transformations of ventral paw structures, as well as subtle alterations along the proximal-distal limb axis. For a review of the role of this gene in limb development, see Johnson and Tabin (1997). Martin et al. (1990) mapped the En1 gene to mouse chromosome 1, approximately 0.28 cM distal to the 'dominant hemimelia' (Dh) gene, and the En2 gene to mouse chromosome 5, approximately 1.1 cM proximal to the 'hemimelic extra-toes' (Hx) gene. They excluded both of these genes as the site of the mutations responsible for Dh and Hx. They suggested that En1/Dh and En2/Hx represent paralogous linkage groups that evolved following duplication of a common ancestral chromosome segment. By Southern analysis of mouse-human somatic cell hybrids, Logan et al. (1989) mapped the human EN1 gene to chromosome 2. Using a mapping panel of rodent/human cell hybrids containing different regions of chromosome 2 and a lymphoblastoid cell line with an interstitial deletion,

del(2)(q21–q23.2), Kohler et al. (1993) refined the regional assignment of EN1 to 2q13–q21. They stated that this increased to 22 the number of known genes on 2q that have homologs in the proximal region of mouse chromosome 1. By fluorescence in situ hybridization, Matsui et al. (1993) further refined the EN1 gene map position to 2q14.

[54876] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54877] Hanks, M.; Wurst, W.; Anson–Cartwright, L.; Auerbach, A. B.; Joyner, A. L. : Rescue of the En–1 mutant phenotype by replacement of En–1 with En–2. Science 269: 679–682, 1995. ; and

[54878] Johnson, R. L.; Tabin, C. J. : Molecular models for vertebrate limb development. Cell 90: 979–990, 1997.

[54879] Further studies establishing the function and utilities of EN1 are found in John Hopkins OMIM database record ID 131290, and in cited publications numbered 2603–2611 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Forkhead Box E1 (thyroid transcription factor 2) (FOXE1, Accession NM\_004473) is another VGAM1615 host target gene.



FOX E1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FOX E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOX E1 BINDING SITE, designated SEQ ID:10781, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54880] Another function of VGAM1615 is therefore inhibition of Forkhead Box E1 (thyroid transcription factor 2) (FOX E1, Accession NM\_004473). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOX E1. Regulatory Factor X, 2 (influences HLA class II expression) (RFX2, Accession NM\_000635) is another VGAM1615 host target gene. RFX2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RFX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX2 BINDING SITE, designated SEQ ID:6271, to the nucleotide sequence of VGAM1615 RNA, herein

designated VGAM RNA, also designated SEQ ID:4326.

[54881] Another function of VGAM1615 is therefore inhibition of Regulatory Factor X, 2 (influences HLA class II expression) (RFX2, Accession NM\_000635), a gene which acts as a dimer to regulate the expression of many genes. Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFX2. The function of RFX2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM622. RAR-related Orphan Receptor B (RORB, Accession NM\_006914) is another VGAM1615 host target gene. RORB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RORB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RORB BINDING SITE, designated SEQ ID:13786, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54882] Another function of VGAM1615 is therefore inhibition of RAR-related Orphan Receptor B (RORB, Accession

NM\_006914), a gene which is an orphan nuclear receptor. Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RORB. The function of RORB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM\_114281) is another VGAM1615 host target gene. SCN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN1A BINDING SITE, designated SEQ ID:42833, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54883] Another function of VGAM1615 is therefore inhibition of Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM\_114281). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN1A.

Cyclin I (CCNI, Accession NM\_006835) is another VGAM1615 host target gene. CCNI BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CCNI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNI BINDING SITE, designated SEQ ID:13713, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54884] Another function of VGAM1615 is therefore inhibition of Cyclin I (CCNI, Accession NM\_006835). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNI. FLJ10099 (Accession NM\_017994) is another VGAM1615 host target gene. FLJ10099 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10099, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10099 BINDING SITE, designated SEQ ID:19725, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM

RNA, also designated SEQ ID:4326.

[54885] Another function of VGAM1615 is therefore inhibition of FLJ10099 (Accession NM\_017994). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10099. FLJ10350 (Accession XM\_170946) is another VGAM1615 host target gene. FLJ10350 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10350 BINDING SITE, designated SEQ ID:45730, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54886] Another function of VGAM1615 is therefore inhibition of FLJ10350 (Accession XM\_170946). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10350. FLJ10846 (Accession NM\_018241) is another VGAM1615 host target gene. FLJ10846 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10846, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10846 BINDING SITE, designated SEQ ID:20198, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54887] Another function of VGAM1615 is therefore inhibition of FLJ10846 (Accession NM\_018241). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10846. KIAA1655 (Accession XM\_039442) is another VGAM1615 host target gene. KIAA1655 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1655 BINDING SITE, designated SEQ ID:33086, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54888] Another function of VGAM1615 is therefore inhibition of KIAA1655 (Accession XM\_039442). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1655. MAGE-E1 (Accession NM\_030801) is another VGAM1615 host target gene. MAGE-E1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAGE-E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAGE-E1 BINDING SITE, designated SEQ ID:25105, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54889] Another function of VGAM1615 is therefore inhibition of MAGE-E1 (Accession NM\_030801). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAGE-E1. MGC15631 (Accession NM\_032753) is another VGAM1615 host target gene. MGC15631 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15631, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15631 BINDING SITE, designated SEQ ID:26492, to

the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54890] Another function of VGAM1615 is therefore inhibition of MGC15631 (Accession NM\_032753). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15631. LOC143920 (Accession XM\_084658) is another VGAM1615 host target gene. LOC143920 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143920 BINDING SITE, designated SEQ ID:37640, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54891] Another function of VGAM1615 is therefore inhibition of LOC143920 (Accession XM\_084658). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143920. LOC164397 (Accession XM\_092780) is another VGAM1615 host target gene. LOC164397 BINDING SITE is HOST TARGET binding site found in the 5' un-



translated region of mRNA encoded by LOC164397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164397 BINDING SITE, designated SEQ ID:40151, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54892] Another function of VGAM1615 is therefore inhibition of LOC164397 (Accession XM\_092780). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164397. LOC220549 (Accession XM\_167521) is another VGAM1615 host target gene. LOC220549 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220549 BINDING SITE, designated SEQ ID:44650, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54893] Another function of VGAM1615 is therefore inhibition of LOC220549 (Accession XM\_167521). Accordingly, utilities

of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220549. LOC220558 (Accession XM\_165930) is another VGAM1615 host target gene. LOC220558 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220558 BINDING SITE, designated SEQ ID:43805, to the nucleotide sequence of VGAM1615 RNA, herein designated VGAM RNA, also designated SEQ ID:4326.

[54894] Another function of VGAM1615 is therefore inhibition of LOC220558 (Accession XM\_165930). Accordingly, utilities of VGAM1615 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220558. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1616 (VGAM1616) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54895] VGAM1616 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1616 was detected is described hereinabove with reference to Figs. 1-8.

[54896] VGAM1616 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1616 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54897] VGAM1616 gene encodes a VGAM1616 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1616 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1616 precursor RNA is designated SEQ ID:1602, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1602 is located at position 2891 relative to the genome of Chimpanzee Cytomegalovirus.

[54898] VGAM1616 precursor RNA folds onto itself, forming VGAM1616 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54899] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1616 folded precursor RNA into VGAM1616 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1616 RNA is designated SEQ ID:4327, and is provided hereinbelow with reference to the sequence listing part.

[54900] VGAM1616 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1616 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1616 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[54901] VGAM1616 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1616 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1616 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1616 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1616 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54902] The complementary binding of VGAM1616 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1616 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1616 host target RNA into VGAM1616 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54903] It is appreciated that VGAM1616 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1616 host target genes. The mRNA of each one of this plurality of VGAM1616 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1616 RNA, herein designated VGAM RNA, and which when bound by VGAM1616 RNA causes inhibition of translation of respective one or more VGAM1616 host target proteins.

[54904] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1616 gene, herein designated VGAM GENE, on one or more VGAM1616 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54905] It is yet further appreciated that a function of VGAM1616 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1616 correlate with, and may be deduced from, the identity of the host target genes which VGAM1616 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54906] Nucleotide sequences of the VGAM1616 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1616 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1616 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1616 are further  
described hereinbelow with reference to Table 1.

[54907] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1616 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1616 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[54908] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1616 gene, herein designated VGAM is  
inhibition of expression of VGAM1616 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1616 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1616  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[54909] A Kinase (PRKA) Anchor Protein 2 (AKAP2, Accession  
NM\_007203) is a VGAM1616 host target gene. AKAP2



BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP2 BINDING SITE, designated SEQ ID:14057, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54910] A function of VGAM1616 is therefore inhibition of A Kinase (PRKA) Anchor Protein 2 (AKAP2, Accession NM\_007203), a gene which binds to regulatory subunit (rii) of protein kinase a. Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP2. The function of AKAP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18. Growth Hormone Receptor (GHR, Accession NM\_000163) is another VGAM1616 host target gene. GHR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GHR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of GHR BINDING SITE, designated SEQ ID:5672, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54911] Another function of VGAM1616 is therefore inhibition of Growth Hormone Receptor (GHR, Accession NM\_000163). Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GHR. Inducible T-cell Co-stimulator (ICOS, Accession NM\_012092) is another VGAM1616 host target gene. ICOS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICOS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICOS BINDING SITE, designated SEQ ID:14387, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54912] Another function of VGAM1616 is therefore inhibition of Inducible T-cell Co-stimulator (ICOS, Accession NM\_012092), a gene which forms homodimers and functions as an inducible T-cell co-stimulator. Accordingly,

utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICOS. The function of ICOS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18. Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM\_003257) is another VGAM1616 host target gene. TJP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TJP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TJP1 BINDING SITE, designated SEQ ID:9263, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54913] Another function of VGAM1616 is therefore inhibition of Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM\_003257), a gene which colocalizes and interacts with cadherins in cells lacking tight junctions. Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TJP1. The function of TJP1 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Rho GTPase Activating Protein 5 (ARHGAP5, Accession XM\_085082) is another VGAM1616 host target gene. ARHGAP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGAP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP5 BINDING SITE, designated SEQ ID:37818, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54914] Another function of VGAM1616 is therefore inhibition of Rho GTPase Activating Protein 5 (ARHGAP5, Accession XM\_085082). Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP5. FLJ12960 (Accession NM\_024638) is another VGAM1616 host target gene. FLJ12960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12960 BINDING SITE, designated SEQ ID:23915, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54915] Another function of VGAM1616 is therefore inhibition of FLJ12960 (Accession NM\_024638). Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12960. KIAA1762 (Accession XM\_033370) is another VGAM1616 host target gene. KIAA1762 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1762, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1762 BINDING SITE, designated SEQ ID:31909, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54916] Another function of VGAM1616 is therefore inhibition of KIAA1762 (Accession XM\_033370). Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1762. MGC15482 (Accession NM\_032875) is another VGAM1616 host target gene. MGC15482 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15482, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15482 BINDING SITE, designated SEQ ID:26695, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54917] Another function of VGAM1616 is therefore inhibition of MGC15482 (Accession NM\_032875). Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15482. LOC124045 (Accession XM\_071873) is another VGAM1616 host target gene. LOC124045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124045 BINDING SITE, designated SEQ ID:37440, to the nucleotide sequence of VGAM1616 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4327.

[54918] Another function of VGAM1616 is therefore inhibition of LOC124045 (Accession XM\_071873). Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124045. LOC143465 (Accession XM\_096430) is another VGAM1616 host target gene. LOC143465 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143465 BINDING SITE, designated SEQ ID:40362, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54919] Another function of VGAM1616 is therefore inhibition of LOC143465 (Accession XM\_096430). Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143465. LOC203378 (Accession XM\_117541) is another VGAM1616 host target gene. LOC203378 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203378, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203378 BINDING SITE, designated SEQ ID:43550, to the nucleotide sequence of VGAM1616 RNA, herein designated VGAM RNA, also designated SEQ ID:4327.

[54920] Another function of VGAM1616 is therefore inhibition of LOC203378 (Accession XM\_117541). Accordingly, utilities of VGAM1616 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203378. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1617 (VGAM1617) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54921] VGAM1617 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1617 was detected is described hereinabove with reference to Figs. 1-8.

[54922] VGAM1617 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl Adenovirus D.



VGAM1617 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54923] VGAM1617 gene encodes a VGAM1617 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1617 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1617 precursor RNA is designated SEQ ID:1603, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1603 is located at position 10492 relative to the genome of Fowl Adenovirus D.

[54924] VGAM1617 precursor RNA folds onto itself, forming VGAM1617 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54925] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1617 folded precursor RNA into VGAM1617 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1617 RNA is designated SEQ ID:4328, and is provided hereinbelow with reference to the sequence listing part.

[54926] VGAM1617 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1617 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1617 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54927] VGAM1617 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1617 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1617 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1617 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1617 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54928] The complementary binding of VGAM1617 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1617 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1617 host target RNA into VGAM1617 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54929] It is appreciated that VGAM1617 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1617 host target genes. The mRNA of each one of this plurality of VGAM1617 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1617 RNA, herein designated VGAM RNA, and which when bound by VGAM1617 RNA causes inhibition of translation of respective one or more VGAM1617 host target proteins.

[54930] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1617 gene, herein designated VGAM GENE, on one or more VGAM1617 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54931] It is yet further appreciated that a function of VGAM1617 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1617 include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific functions, and accordingly utilities, of VGAM1617 correlate with, and may be deduced from, the identity of the host target genes which VGAM1617 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54932] Nucleotide sequences of the VGAM1617 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1617 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1617 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1617 are further described hereinbelow with reference to Table 1.

[54933] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1617 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1617 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54934] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1617 gene, herein designated VGAM is inhibition of expression of VGAM1617 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1617 correlate with, and may be deduced from, the identity of the target genes which VGAM1617 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54935] LOC257463 (Accession XM\_048605) is a VGAM1617 host target gene. LOC257463 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257463 BINDING SITE, designated SEQ ID:35208, to the nucleotide sequence of

VGAM1617 RNA, herein designated VGAM RNA, also designated SEQ ID:4328.

[54936] A function of VGAM1617 is therefore inhibition of LOC257463 (Accession XM\_048605). Accordingly, utilities of VGAM1617 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257463. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1618 (VGAM1618) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54937] VGAM1618 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1618 was detected is described hereinabove with reference to Figs. 1–8.

[54938] VGAM1618 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl Adenovirus D. VGAM1618 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54939] VGAM1618 gene encodes a VGAM1618 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1618 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1618 precursor RNA is designated SEQ ID:1604, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1604 is located at position 5025 relative to the genome of Fowl Adenovirus D.

[54940] VGAM1618 precursor RNA folds onto itself, forming VGAM1618 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54941] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1618 folded precursor RNA into VGAM1618 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1618 RNA is designated SEQ ID:4329, and is provided hereinbelow with reference to the sequence listing part.

[54942] VGAM1618 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1618 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1618 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54943] VGAM1618 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1618 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1618 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1618 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1618 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54944] The complementary binding of VGAM1618 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1618 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1618 host target RNA into VGAM1618 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54945] It is appreciated that VGAM1618 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1618 host target genes. The mRNA of each one of this plurality of VGAM1618 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1618 RNA, herein designated VGAM RNA, and which when bound by VGAM1618 RNA causes inhibition of translation of respective one or more VGAM1618 host target proteins.

[54946] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1618 gene, herein designated VGAM GENE, on one or more VGAM1618 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[54947] It is yet further appreciated that a function of VGAM1618 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1618 include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific functions, and accordingly utilities, of VGAM1618 correlate with, and may be deduced from, the identity of the host target genes which VGAM1618 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54948] Nucleotide sequences of the VGAM1618 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1618 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1618 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1618 are further described hereinbelow with reference to Table 1.

[54949] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1618 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1618 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54950] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1618 gene, herein designated VGAM is inhibition of expression of VGAM1618 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1618 correlate with, and may be deduced from, the identity of the target genes which VGAM1618 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54951] Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM\_014837) is a VGAM1618 host target gene. C1orf16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf16 BINDING SITE, designated SEQ ID:16855, to the nucleotide sequence of VGAM1618 RNA, herein designated VGAM RNA, also designated SEQ ID:4329.

[54952] A function of VGAM1618 is therefore inhibition of Chro-

Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM\_014837). Accordingly, utilities of VGAM1618 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf16. Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM\_032385) is another VGAM1618 host target gene. C5orf4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C5orf4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf4 BINDING SITE, designated SEQ ID:26182, to the nucleotide sequence of VGAM1618 RNA, herein designated VGAM RNA, also designated SEQ ID:4329.

[54953] Another function of VGAM1618 is therefore inhibition of Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM\_032385). Accordingly, utilities of VGAM1618 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf4. DKFZP586J0619 (Accession XM\_088280) is another VGAM1618 host target gene. DKFZP586J0619 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586J0619, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586J0619 BINDING SITE, designated SEQ ID:39580, to the nucleotide sequence of VGAM1618 RNA, herein designated VGAM RNA, also designated SEQ ID:4329.

[54954] Another function of VGAM1618 is therefore inhibition of DKFZP586J0619 (Accession XM\_088280). Accordingly, utilities of VGAM1618 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586J0619. LOC161244 (Accession XM\_101700) is another VGAM1618 host target gene. LOC161244 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC161244, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161244 BINDING SITE, designated SEQ ID:42107, to the nucleotide sequence of VGAM1618 RNA, herein designated VGAM RNA, also designated SEQ ID:4329.

[54955] Another function of VGAM1618 is therefore inhibition of LOC161244 (Accession XM\_101700). Accordingly, utilities

of VGAM1618 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161244. LOC255718 (Accession XM\_174148) is another VGAM1618 host target gene. LOC255718 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255718, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255718 BINDING SITE, designated SEQ ID:46580, to the nucleotide sequence of VGAM1618 RNA, herein designated VGAM RNA, also designated SEQ ID:4329.

[54956] Another function of VGAM1618 is therefore inhibition of LOC255718 (Accession XM\_174148). Accordingly, utilities of VGAM1618 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255718. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1619 (VGAM1619) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[54957] VGAM1619 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1619 was detected is described hereinabove with reference to Figs. 1–8.

[54958] VGAM1619 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl Adenovirus D. VGAM1619 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54959] VGAM1619 gene encodes a VGAM1619 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1619 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1619 precursor RNA is designated SEQ ID:1605, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1605 is located at position 4810 relative to the genome of Fowl Adenovirus D.

[54960] VGAM1619 precursor RNA folds onto itself, forming VGAM1619 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54961] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1619 folded precursor RNA into VGAM1619 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1619 RNA is designated SEQ ID:4330, and is provided hereinbelow with reference to the sequence listing part.

[54962] VGAM1619 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1619 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1619 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[54963] VGAM1619 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1619 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1619 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1619 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1619 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54964] The complementary binding of VGAM1619 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1619 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1619 host target RNA into VGAM1619 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54965] It is appreciated that VGAM1619 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1619 host target genes. The mRNA of each one of this plurality of VGAM1619 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1619 RNA, herein designated VGAM RNA, and which when bound by VGAM1619 RNA causes inhibition of translation of respective one or more VGAM1619 host target proteins.

[54966] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1619 gene, herein designated VGAM GENE, on one or more VGAM1619 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54967] It is yet further appreciated that a function of VGAM1619 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1619 include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific functions, and accordingly utilities, of VGAM1619 correlate with, and may be deduced from, the identity of the host target genes which VGAM1619 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54968] Nucleotide sequences of the VGAM1619 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1619 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1619 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1619 are further  
described hereinbelow with reference to Table 1.

[54969] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1619 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1619 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[54970] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1619 gene, herein designated VGAM is  
inhibition of expression of VGAM1619 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1619 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1619  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[54971] Snail Homolog 1 (Drosophila) (SNAI1, Accession  
NM\_005985) is a VGAM1619 host target gene. SNAI1

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNAI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAI1 BINDING SITE, designated SEQ ID:12607, to the nucleotide sequence of VGAM1619 RNA, herein designated VGAM RNA, also designated SEQ ID:4330.

[54972] A function of VGAM1619 is therefore inhibition of Snail Homolog 1 (Drosophila) (SNAI1, Accession NM\_005985). Accordingly, utilities of VGAM1619 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAI1. PIPPIN (Accession XM\_086825) is another VGAM1619 host target gene. PIPPIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIPPIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIPPIN BINDING SITE, designated SEQ ID:38909, to the nucleotide sequence of VGAM1619 RNA, herein designated VGAM RNA, also designated SEQ ID:4330.

[54973] Another function of VGAM1619 is therefore inhibition of PIPPIN (Accession XM\_086825). Accordingly, utilities of VGAM1619 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIPPIN. Voltage-dependent Anion Channel 3 (VDAC3, Accession NM\_005662) is another VGAM1619 host target gene. VDAC3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VDAC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VDAC3 BINDING SITE, designated SEQ ID:12203, to the nucleotide sequence of VGAM1619 RNA, herein designated VGAM RNA, also designated SEQ ID:4330.

[54974] Another function of VGAM1619 is therefore inhibition of Voltage-dependent Anion Channel 3 (VDAC3, Accession NM\_005662). Accordingly, utilities of VGAM1619 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VDAC3. LOC255452 (Accession XM\_174088) is another VGAM1619 host target gene. LOC255452 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded



by LOC255452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255452 BINDING SITE, designated SEQ ID:46572, to the nucleotide sequence of VGAM1619 RNA, herein designated VGAM RNA, also designated SEQ ID:4330.

[54975] Another function of VGAM1619 is therefore inhibition of LOC255452 (Accession XM\_174088). Accordingly, utilities of VGAM1619 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255452. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1620 (VGAM1620) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[54976] VGAM1620 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1620 was detected is described hereinabove with reference to Figs. 1-8.

[54977] VGAM1620 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Fowl Adenovirus D. VGAM1620 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[54978] VGAM1620 gene encodes a VGAM1620 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1620 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1620 precursor RNA is designated SEQ ID:1606, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1606 is located at position 9503 relative to the genome of Fowl Adenovirus D.

[54979] VGAM1620 precursor RNA folds onto itself, forming VGAM1620 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[54980] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1620 folded precursor RNA into VGAM1620 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1620 RNA is designated SEQ ID:4331, and is provided hereinbelow with reference to the sequence listing part.

[54981] VGAM1620 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1620 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1620 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[54982] VGAM1620 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1620 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1620 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1620 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1620 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[54983] The complementary binding of VGAM1620 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1620 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1620

host target RNA into VGAM1620 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[54984] It is appreciated that VGAM1620 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1620 host target genes. The mRNA of each one of this plurality of VGAM1620 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1620 RNA, herein designated VGAM RNA, and which when bound by VGAM1620 RNA causes inhibition of translation of respective one or more VGAM1620 host target proteins.

[54985] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1620 gene, herein designated VGAM GENE, on one or more VGAM1620 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[54986] It is yet further appreciated that a function of VGAM1620 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1620 include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific functions, and accordingly utilities, of VGAM1620 correlate with, and may be deduced from, the identity of the host target genes which VGAM1620 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[54987] Nucleotide sequences of the VGAM1620 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1620 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1620 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1620 are further

described hereinbelow with reference to Table 1.

[54988] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1620 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1620 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[54989] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1620 gene, herein designated VGAM is inhibition of expression of VGAM1620 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1620 correlate with, and may be deduced from, the identity of the target genes which VGAM1620 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[54990] Isoleucine-tRNA Synthetase (IARS, Accession NM\_013417) is a VGAM1620 host target gene. IARS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IARS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IARS BINDING

SITE, designated SEQ ID:15080, to the nucleotide sequence of VGAM1620 RNA, herein designated VGAM RNA, also designated SEQ ID:4331.

[54991] A function of VGAM1620 is therefore inhibition of Isoleucine-tRNA Synthetase (IARS, Accession NM\_013417), a gene which functions in protein biosynthesis. Accordingly, utilities of VGAM1620 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IARS. The function of IARS has been established by previous studies. The autoimmune diseases polymyositis and dermatomyositis are a consequence of autoantibodies directed against 1 or more of the aminoacyl-tRNA synthetases with subsequent lymphocytic destruction of myocytes. Nichols et al. (1995) cloned the cDNA for isoleucyl-tRNA synthetase (TRIS, which they referred to as IRS) by using autoantibodies from patients to purify the protein. Partial amino acid sequence was obtained from tryptic peptides and DNA probes were designed and used to screen liver and HeLa cell libraries. The cDNA has a 1,262-amino acid reading frame with significant sequence similarity to isoleucyl-tRNA synthetases from both yeast and Tetrahymena. The predicted protein contains the expected motifs of class-I hydropho-



bic aminoacyl-tRNA synthetases and the human protein has a C-terminal domain not seen in the lower organisms. The human gene can produce 2 alternatively spliced mRNAs based on the use of a 5-prime untranslated exon. Nichols et al. (1995) speculated that the autoantibodies produced in patients may recognize an epitope in this region. Six of 20 human aminoacyl-tRNA synthetases have been identified as targets of autoantibodies in the autoimmune disease polymyositis/dermatomyositis: histidyl-RS (OMIM Ref. No. 142810) on chromosome 5, threonyl-RS (OMIM Ref. No. 187790), also on chromosome 5, alanyl-RS (OMIM Ref. No. 601065) on chromosome 16, glycyl-RS (OMIM Ref. No. 600287) on chromosome 7, isoleucyl-RS, and lysyl-RS (OMIM Ref. No. 601421). By PCR-based analysis of a human/rodent somatic cell hybrid panel, Nichols et al. (1996) assigned IARS to chromosome 9. By fluorescence in situ hybridization analysis, they regionalized the IARS gene to 9q21.

[54992] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[54993] Nichols, R. C.; Blinder, J.; Pai, S. I.; Ge, Q.; Targoff, I. N.; Plotz, P. H.; Liu, P. : Assignment of two human autoanti-

gen genes: isoleucyl-tRNA synthetase locates to 9q21 and lysyl-tRNA synthetase locates to 16q23-q24. Genomics 36: 210-213, 1996. ; and

[54994] Nichols, R. C.; Raben, N.; Boerkoel, C. F.; Plotz, P. H. : Human isoleucyl-tRNA synthetase: sequence of the cDNA, alternative mRNA splicing, and the characteristics of an unusually long.

[54995] Further studies establishing the function and utilities of IARS are found in John Hopkins OMIM database record ID 600709, and in cited publications numbered 10047-10048 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0795 (Accession NM\_025010) is another VGAM1620 host target gene. KIAA0795 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0795 BINDING SITE, designated SEQ ID:24583, to the nucleotide sequence of VGAM1620 RNA, herein designated VGAM RNA, also designated SEQ ID:4331.

[54996] Another function of VGAM1620 is therefore inhibition of

KIAA0795 (Accession NM\_025010). Accordingly, utilities of VGAM1620 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0795. LOC145693 (Accession XM\_085205) is another VGAM1620 host target gene. LOC145693 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145693 BINDING SITE, designated SEQ ID:37922, to the nucleotide sequence of VGAM1620 RNA, herein designated VGAM RNA, also designated SEQ ID:4331.

[54997] Another function of VGAM1620 is therefore inhibition of LOC145693 (Accession XM\_085205). Accordingly, utilities of VGAM1620 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145693. LOC254431 (Accession XM\_173024) is another VGAM1620 host target gene. LOC254431 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254431, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC254431 BINDING SITE, designated SEQ ID:46293, to the nucleotide sequence of VGAM1620 RNA, herein designated VGAM RNA, also designated SEQ ID:4331.

[54998] Another function of VGAM1620 is therefore inhibition of LOC254431 (Accession XM\_173024). Accordingly, utilities of VGAM1620 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254431. LOC90591 (Accession XM\_032811) is another VGAM1620 host target gene. LOC90591 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90591, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90591 BINDING SITE, designated SEQ ID:31760, to the nucleotide sequence of VGAM1620 RNA, herein designated VGAM RNA, also designated SEQ ID:4331.

[54999] Another function of VGAM1620 is therefore inhibition of LOC90591 (Accession XM\_032811). Accordingly, utilities of VGAM1620 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90591. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1621 (VGAM1621) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55000] VGAM1621 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1621 was detected is described hereinabove with reference to Figs. 1–8.

[55001] VGAM1621 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl Adenovirus D. VGAM1621 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55002] VGAM1621 gene encodes a VGAM1621 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1621 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1621 precursor RNA is designated SEQ ID:1607, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1607 is located at position 4619 relative to the genome of Fowl Adenovirus D.

[55003] VGAM1621 precursor RNA folds onto itself, forming VGAM1621 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55004] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1621 folded precursor RNA into VGAM1621 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1621 RNA is designated SEQ ID:4332, and is provided hereinbelow with reference to the sequence listing part.

[55005] VGAM1621 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1621 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1621 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[55006] VGAM1621 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1621 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1621 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1621 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1621 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[55007] The complementary binding of VGAM1621 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1621 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1621 host target RNA into VGAM1621 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55008] It is appreciated that VGAM1621 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1621 host target genes. The mRNA of each one of this plurality of VGAM1621 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1621 RNA, herein designated VGAM RNA, and which when bound by VGAM1621 RNA causes inhibition of translation of respective one or more



VGAM1621 host target proteins.

[55009] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1621 gene, herein designated VGAM GENE, on one or more VGAM1621 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55010] It is yet further appreciated that a function of VGAM1621 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific

functions, and accordingly utilities, of VGAM1621 correlate with, and may be deduced from, the identity of the host target genes which VGAM1621 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55011] Nucleotide sequences of the VGAM1621 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1621 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1621 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1621 are further described hereinbelow with reference to Table 1.

[55012] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1621 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1621 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55013] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1621 gene, herein designated VGAM is inhibition of expression of VGAM1621 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1621 correlate with, and may be deduced from, the identity of the target genes which VGAM1621 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55014] Citron (rho-interacting, serine/threonine kinase 21) (CIT, Accession XM\_045786) is a VGAM1621 host target gene. CIT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CIT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CIT BINDING SITE, designated SEQ ID:34563, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55015] A function of VGAM1621 is therefore inhibition of Citron (rho-interacting, serine/threonine kinase 21) (CIT, Accession XM\_045786), a gene which is increased several-fold by coexpression of constitutively active Rho . Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CIT. The function of CIT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with refer-

ence to VGAM393.Carnitine Acetyltransferase (CRAT, Accession NM\_004003) is another VGAM1621 host target gene. CRAT BINDING SITE1 and CRAT BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CRAT, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRAT BINDING SITE1 and CRAT BINDING SITE2, designated SEQ ID:10152 and SEQ ID:6407 respectively, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55016] Another function of VGAM1621 is therefore inhibition of Carnitine Acetyltransferase (CRAT, Accession NM\_004003), a gene which catalyzes the reversible transfer of acyl groups from an acyl-CoA thioester to carnitine. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRAT. The function of CRAT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189.DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 3 (DDX3, Acces-

sion NM\_024005) is another VGAM1621 host target gene. DDX3 BINDING SITE1 and DDX3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DDX3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX3 BINDING SITE1 and DDX3 BINDING SITE2, designated SEQ ID:23434 and SEQ ID:7649 respectively, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55017] Another function of VGAM1621 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 3 (DDX3, Accession NM\_024005), a gene which interacts with hepatitis c virus core protein resulting a change in intracellular location. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX3. The function of DDX3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. Eukaryotic Translation Initiation Factor 4 Gamma, 1 (EIF4G1, Accession NM\_004953) is another

VGAM1621 host target gene. EIF4G1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by EIF4G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4G1 BINDING SITE, designated SEQ ID:11397, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55018] Another function of VGAM1621 is therefore inhibition of Eukaryotic Translation Initiation Factor 4 Gamma, 1 (EIF4G1, Accession NM\_004953), a gene which is a Translation initiation factor. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF4G1. The function of EIF4G1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1403.EphA2 (EPHA2, Accession NM\_004431) is another VGAM1621 host target gene. EPHA2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EPHA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA2 BINDING SITE, designated SEQ ID:10716, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55019] Another function of VGAM1621 is therefore inhibition of EphA2 (EPHA2, Accession NM\_004431), a gene which binds to ephrin-a1, -a3, -a4 and -a5. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA2. The function of EPHA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1289. Insulin-like Growth Factor Binding Protein 5 (IGFBP5, Accession NM\_000599) is another VGAM1621 host target gene. IGFBP5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IGFBP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGFBP5 BINDING SITE, designated SEQ ID:6202, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA,

also designated SEQ ID:4332.

[55020] Another function of VGAM1621 is therefore inhibition of Insulin-like Growth Factor Binding Protein 5 (IGFBP5, Accession NM\_000599), a gene which either inhibits or stimulates the growth promoting effects of the igfs on cell culture. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGFBP5. The function of IGFBP5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1233. Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM\_002507) is another VGAM1621 host target gene. NGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGFR BINDING SITE, designated SEQ ID:8332, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55021] Another function of VGAM1621 is therefore inhibition of



Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM\_002507), a gene which can mediate cell survival as well as cell death of neural cells. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGFR. The function of NGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM212.P21/Cdc42/Rac1-activated Kinase 1 (STE20 homolog, yeast) (PAK1, Accession NM\_002576) is another VGAM1621 host target gene. PAK1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PAK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAK1 BINDING SITE, designated SEQ ID:8435, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55022] Another function of VGAM1621 is therefore inhibition of P21/Cdc42/Rac1-activated Kinase 1 (STE20 homolog, yeast) (PAK1, Accession NM\_002576), a gene which acti-

vates the Jun N-terminal kinase MAP kinase pathway. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK1. The function of PAK1 has been established by previous studies. PAK1 protein promotes the disassembly of stress fibers and focal adhesions. Sanders et al. (1999) demonstrated that, in baby hamster kidney-21 and HeLa cells expressing constitutively active PAK1, MLCK (OMIM Ref. No. 600922) activity and myosin light-chain phosphorylation were decreased, and cell spreading was inhibited. These results indicated that MLCK is a target for PAK1, and that PAKs may regulate cytoskeletal dynamics by decreasing MLCK activity and myosin light-chain phosphorylation. Parrini et al. (2002) showed that PAK1 forms homodimers in vivo and that its dimerization is regulated by the intracellular level of GTP-CDC42 (OMIM Ref. No. 116952) or GTP-RAC1 (OMIM Ref. No. 602048). The dimerized PAK1 adopts a trans-inhibited conformation: the N-terminal inhibitory portion of one PAK1 molecule in the dimer binds and inhibits the catalytic domain of the other. One GTPase interaction can result in activation of both partners. Another ligand, beta-PIX (OMIM Ref. No. 605477), can stably associate with

dimerized PAK1. Dimerization does not facilitate PAK1 trans-phosphorylation. The authors concluded that the functional significance of dimerization is to allow trans-inhibition. Vadlamudi et al. (2002) identified filamin A (FLNA; 300017) as a binding partner of PAK1 in a yeast 2-hybrid screen of a mammary gland cDNA library. By mutation analysis, they localized the PAK1-binding region in FLNA to tandem repeat 23 in the C terminus, and the FLNA-binding region in PAK1 between amino acids 52 and 132 in the conserved CDC42 (OMIM Ref. No. 116952)/RAC (OMIM Ref. No. 602048)-interacting domain. Endogenous FLNA was phosphorylated by PAK1 on ser2152 following stimulation with physiologic signaling molecules. Following stimulation, FLNA colocalized with PAK1 in membrane ruffles. The ruffle-forming activity of PAK1 was found in FLNA-expressing cells, but not in cells deficient in FLNA.

[55023] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55024] Sanders, L. C.; Matsumura, F.; Bokoch, G. M.; de Lanerolle, P. : Inhibition of myosin light chain kinase by p21-activated kinase. Science 283: 2083-2085, 1999. ; and

[55025] Vadlamudi, R. K.; Li, F.; Adam, L.; Nguyen, D.; Ohta, Y.; Stossel, T. P.; Kumar, R. : Filamin is essential in actin cytoskeletal assembly mediated by p21-activated kinase 1. Nature Cell.

[55026] Further studies establishing the function and utilities of PAK1 are found in John Hopkins OMIM database record ID 602590, and in cited publications numbered 8637-1035, 1039-104 and 7264 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_030668) is another VGAM1621 host target gene. PTPRO BINDING SITE1 through PTPRO BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRO, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE1 through PTPRO BINDING SITE3, designated SEQ ID:25010, SEQ ID:25019 and SEQ ID:25029 respectively, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55027] Another function of VGAM1621 is therefore inhibition of

Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_030668), a gene which may function as a cell contact receptor that mediates and controls cell-cell signals. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM140. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1 (SMARCD1, Accession NM\_139071) is another VGAM1621 host target gene.

SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMARCD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2, designated SEQ ID:29144 and SEQ ID:9046 respectively, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55028] Another function of VGAM1621 is therefore inhibition of

SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1

(SMARCD1, Accession NM\_139071), a gene which is involved in chromatin assembly and remodeling. Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCD1. The function of SMARCD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Chromosome 11

Open Reading Frame 9 (C11orf9, Accession NM\_013279) is another VGAM1621 host target gene. C11orf9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C11orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf9 BINDING SITE, designated SEQ ID:14944, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55029] Another function of VGAM1621 is therefore inhibition of Chromosome 11 Open Reading Frame 9 (C11orf9, Accession NM\_013279). Accordingly, utilities of VGAM1621 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf9. Centaurin, Gamma 1 (CENTG1, Accession NM\_014770) is another VGAM1621 host target gene. CENTG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTG1 BINDING SITE, designated SEQ ID:16566, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55030] Another function of VGAM1621 is therefore inhibition of Centaurin, Gamma 1 (CENTG1, Accession NM\_014770). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTG1. Claudin 6 (CLDN6, Accession NM\_021195) is another VGAM1621 host target gene. CLDN6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLDN6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of CLDN6 BINDING SITE, designated SEQ ID:22170, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55031] Another function of VGAM1621 is therefore inhibition of Claudin 6 (CLDN6, Accession NM\_021195). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLDN6. Diacylglycerol Kinase, Zeta 104kDa (DGKZ, Accession NM\_003646) is another VGAM1621 host target gene. DGKZ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGKZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKZ BINDING SITE, designated SEQ ID:9719, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55032] Another function of VGAM1621 is therefore inhibition of Diacylglycerol Kinase, Zeta 104kDa (DGKZ, Accession NM\_003646). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKZ. DKFZP586P0123



(Accession XM\_170681) is another VGAM1621 host target gene. DKFZP586P0123 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP586P0123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586P0123 BINDING SITE, designated SEQ ID:45464, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55033] Another function of VGAM1621 is therefore inhibition of DKFZP586P0123 (Accession XM\_170681). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586P0123. Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295) is another VGAM1621 host target gene. EPB41L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EPB41L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L1 BINDING SITE, designated SEQ ID:34944, to the nucleotide

sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55034] Another function of VGAM1621 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L1. FLJ13102 (Accession NM\_024887) is another VGAM1621 host target gene. FLJ13102 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13102, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13102 BINDING SITE, designated SEQ ID:24343, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55035] Another function of VGAM1621 is therefore inhibition of FLJ13102 (Accession NM\_024887). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13102. FLJ13840 (Accession NM\_024746) is another VGAM1621 host target gene. FLJ13840 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ13840, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13840 BINDING SITE, designated SEQ ID:24081, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55036] Another function of VGAM1621 is therefore inhibition of FLJ13840 (Accession NM\_024746). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13840. FLJ23040 (Accession NM\_025174) is another VGAM1621 host target gene. FLJ23040 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23040 BINDING SITE, designated SEQ ID:24808, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55037] Another function of VGAM1621 is therefore inhibition of

FLJ23040 (Accession NM\_025174). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23040. GMPPB (Accession XM\_171044) is another VGAM1621 host target gene. GMPPB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GMPPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GMPPB BINDING SITE, designated SEQ ID:45813, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55038] Another function of VGAM1621 is therefore inhibition of GMPPB (Accession XM\_171044). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMPPB. Glycoprotein A33 (transmembrane) (GPA33, Accession NM\_005814) is another VGAM1621 host target gene. GPA33 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPA33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of GPA33 BINDING SITE, designated SEQ ID:12406, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55039] Another function of VGAM1621 is therefore inhibition of Glycoprotein A33 (transmembrane) (GPA33, Accession NM\_005814). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPA33. KIAA0720 (Accession XM\_030970) is another VGAM1621 host target gene. KIAA0720 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0720 BINDING SITE, designated SEQ ID:31233, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55040] Another function of VGAM1621 is therefore inhibition of KIAA0720 (Accession XM\_030970). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0720. KIAA1257 (Accession XM\_031577) is another VGAM1621 host target gene. KIAA1257 BINDING SITE1 and KIAA1257 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1257, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1257 BINDING SITE1 and KIAA1257 BINDING SITE2, designated SEQ ID:31432 and SEQ ID:31434 respectively, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55041] Another function of VGAM1621 is therefore inhibition of KIAA1257 (Accession XM\_031577). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1257. KIAA1649 (Accession NM\_032311) is another VGAM1621 host target gene. KIAA1649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1649 BINDING SITE, designated SEQ ID:26106, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55042] Another function of VGAM1621 is therefore inhibition of KIAA1649 (Accession NM\_032311). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1649. KIAA1822 (Accession XM\_041566) is another VGAM1621 host target gene. KIAA1822 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1822, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1822 BINDING SITE, designated SEQ ID:33556, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55043] Another function of VGAM1621 is therefore inhibition of KIAA1822 (Accession XM\_041566). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1822. KIAA1853 (Accession XM\_045184) is another VGAM1621 host target gene. KIAA1853 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1853, corresponding to a HOST TARGET binding site such as BINDING SITE I,



BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1853 BINDING SITE, designated SEQ ID:34385, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55044] Another function of VGAM1621 is therefore inhibition of KIAA1853 (Accession XM\_045184). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1853. KIAA1944 (Accession XM\_062545) is another VGAM1621 host target gene. KIAA1944 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1944, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1944 BINDING SITE, designated SEQ ID:37228, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55045] Another function of VGAM1621 is therefore inhibition of KIAA1944 (Accession XM\_062545). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1944. MGC2477 (Accession NM\_024099) is another VGAM1621 host target gene. MGC2477 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2477 BINDING SITE, designated SEQ ID:23545, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55046] Another function of VGAM1621 is therefore inhibition of MGC2477 (Accession NM\_024099). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2477. Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM\_015550) is another VGAM1621 host target gene. OSBPL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL3 BINDING SITE, designated SEQ ID:17816, to the nucleotide sequence of VGAM1621 RNA,

herein designated VGAM RNA, also designated SEQ ID:4332.

[55047] Another function of VGAM1621 is therefore inhibition of Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM\_015550). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL3. TSPAN-5 (Accession NM\_005723) is another VGAM1621 host target gene. TSPAN-5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TSPAN-5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSPAN-5 BINDING SITE, designated SEQ ID:12275, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55048] Another function of VGAM1621 is therefore inhibition of TSPAN-5 (Accession NM\_005723). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSPAN-5. VILL (Accession XM\_043435) is another VGAM1621 host target gene. VILL BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by VILL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VILL BINDING SITE, designated SEQ ID:33946, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55049] Another function of VGAM1621 is therefore inhibition of VILL (Accession XM\_043435). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VILL. LOC112616 (Accession NM\_138410) is another VGAM1621 host target gene. LOC112616 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112616, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112616 BINDING SITE, designated SEQ ID:28773, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55050] Another function of VGAM1621 is therefore inhibition of

LOC112616 (Accession NM\_138410). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112616. LOC126528 (Accession XM\_059052) is another VGAM1621 host target gene. LOC126528 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC126528, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126528 BINDING SITE, designated SEQ ID:36843, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55051] Another function of VGAM1621 is therefore inhibition of LOC126528 (Accession XM\_059052). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126528. LOC146268 (Accession XM\_085397) is another VGAM1621 host target gene. LOC146268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC146268 BINDING SITE, designated SEQ ID:38122, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55052] Another function of VGAM1621 is therefore inhibition of LOC146268 (Accession XM\_085397). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146268. LOC147165 (Accession XM\_097205) is another VGAM1621 host target gene. LOC147165 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147165, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147165 BINDING SITE, designated SEQ ID:40813, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55053] Another function of VGAM1621 is therefore inhibition of LOC147165 (Accession XM\_097205). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147165. LOC153020 (Accession XM\_087578) is an-

other VGAM1621 host target gene. LOC153020 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153020 BINDING SITE, designated SEQ ID:39355, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55054] Another function of VGAM1621 is therefore inhibition of LOC153020 (Accession XM\_087578). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153020. LOC222237 (Accession XM\_168592) is another VGAM1621 host target gene. LOC222237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222237 BINDING SITE, designated SEQ ID:45268, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55055] Another function of VGAM1621 is therefore inhibition of LOC222237 (Accession XM\_168592). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222237. LOC253868 (Accession XM\_170975) is another VGAM1621 host target gene. LOC253868 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253868, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253868 BINDING SITE, designated SEQ ID:45748, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55056] Another function of VGAM1621 is therefore inhibition of LOC253868 (Accession XM\_170975). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253868. LOC51246 (Accession NM\_016479) is another VGAM1621 host target gene. LOC51246 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51246, corresponding to a HOST TARGET binding site such as BINDING



SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51246 BINDING SITE, designated SEQ ID:18578, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55057] Another function of VGAM1621 is therefore inhibition of LOC51246 (Accession NM\_016479). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51246. LOC51667 (Accession NM\_016118) is another VGAM1621 host target gene. LOC51667 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51667, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51667 BINDING SITE, designated SEQ ID:18197, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55058] Another function of VGAM1621 is therefore inhibition of LOC51667 (Accession NM\_016118). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC51667. LOC92223 (Accession XM\_043674) is another VGAM1621 host target gene. LOC92223 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92223, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92223 BINDING SITE, designated SEQ ID:33993, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55059] Another function of VGAM1621 is therefore inhibition of LOC92223 (Accession XM\_043674). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92223. LOC93259 (Accession XM\_050105) is another VGAM1621 host target gene. LOC93259 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93259, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93259 BINDING SITE, designated SEQ ID:35562, to the nucleotide sequence of VGAM1621 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4332.

[55060] Another function of VGAM1621 is therefore inhibition of LOC93259 (Accession XM\_050105). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93259. LOC93512 (Accession XM\_051758) is another VGAM1621 host target gene. LOC93512 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93512, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93512 BINDING SITE, designated SEQ ID:35877, to the nucleotide sequence of VGAM1621 RNA, herein designated VGAM RNA, also designated SEQ ID:4332.

[55061] Another function of VGAM1621 is therefore inhibition of LOC93512 (Accession XM\_051758). Accordingly, utilities of VGAM1621 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93512. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1622 (VGAM1622) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55062] VGAM1622 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1622 was detected is described hereinabove with reference to Figs. 1–8.

[55063] VGAM1622 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1622 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55064] VGAM1622 gene encodes a VGAM1622 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1622 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1622 precursor RNA is designated SEQ ID:1608, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1608 is located at position 87319 relative to the genome of Bovine Herpesvirus 4.

[55065] VGAM1622 precursor RNA folds onto itself, forming

VGAM1622 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55066] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1622 folded precursor RNA into VGAM1622 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1622 RNA is designated SEQ ID:4333, and is provided hereinbelow with reference to the sequence listing part.

[55067] VGAM1622 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1622 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1622 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55068] VGAM1622 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1622 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1622 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1622 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1622 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55069] The complementary binding of VGAM1622 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1622 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1622 host target RNA into VGAM1622 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55070] It is appreciated that VGAM1622 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1622 host target genes. The mRNA of each one of this plurality of VGAM1622 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1622 RNA, herein designated VGAM RNA, and which when bound by VGAM1622 RNA causes inhibition of translation of respective one or more VGAM1622 host target proteins.

[55071] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1622 gene, herein designated VGAM GENE, on one or more VGAM1622 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55072] It is yet further appreciated that a function of VGAM1622 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1622 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1622 correlate with, and may be deduced from, the identity of the host target genes which VGAM1622 binds and in-



hibits, and the function of these host target genes, as elaborated hereinbelow.

[55073] Nucleotide sequences of the VGAM1622 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1622 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1622 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1622 are further described hereinbelow with reference to Table 1.

[55074] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1622 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1622 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55075] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1622 gene, herein designated VGAM is inhibition of expression of VGAM1622 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1622 correlate with, and may be deduced from, the identity of the target genes which VGAM1622 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[55076] Calcium/calmodulin-dependent Protein Kinase IV (CAMK4, Accession NM\_001744) is a VGAM1622 host target gene. CAMK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMK4 BINDING SITE, designated SEQ ID:7483, to the nucleotide sequence of VGAM1622 RNA, herein designated VGAM RNA, also designated SEQ ID:4333.

[55077] A function of VGAM1622 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase IV (CAMK4, Accession NM\_001744), a gene which is a heat-stable, acidic, calmodulin-binding protein. Accordingly, utilities of VGAM1622 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMK4. The function of CAMK4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM578. Death Effector Domain Containing (DEDD, Accession NM\_032998) is another VGAM1622 host

target gene. DEDD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DEDD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEDD BINDING SITE, designated SEQ ID:26882, to the nucleotide sequence of VGAM1622 RNA, herein designated VGAM RNA, also designated SEQ ID:4333.

[55078] Another function of VGAM1622 is therefore inhibition of Death Effector Domain Containing (DEDD, Accession NM\_032998), a gene which intervenes in apoptosis. Accordingly, utilities of VGAM1622 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DEDD. The function of DEDD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189. Mitogen-activated Protein Kinase Kinase Kinase 5 (MAP3K5, Accession NM\_005923) is another VGAM1622 host target gene. MAP3K5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K5, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K5 BINDING SITE, designated SEQ ID:12545, to the nucleotide sequence of VGAM1622 RNA, herein designated VGAM RNA, also designated SEQ ID:4333.

[55079] Another function of VGAM1622 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 5 (MAP3K5, Accession NM\_005923), a gene which phosphorylates and activates two different subgroups of map kinase kinases, mkk4/sek1 and mkk3/mapkk6 (or mkk6). overexpression induces apoptotic cell death. Accordingly, utilities of VGAM1622 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K5. The function of MAP3K5 has been established by previous studies. Mitogen-activated protein kinase (MAPK) signaling cascades include MAPK or extracellular signal-regulated kinase (ERK), MAPK kinase (MAP2K, also called MKK or MEK), and MAPK kinase kinase (MAP3K, also called MAPKKK or MEKK). MAPKK kinase/MEKK phosphorylates and activates its downstream protein kinase, MAPK kinase/MEK, which in turn activates MAPK. The kinases of these signaling cascades are highly conserved,

and homologs exist in yeast, *Drosophila*, and mammalian cells Ichijo et al. (1997) used a similar cloning strategy to identify a nearly identical MAPKKK cDNA, termed ASK1 for apoptosis signal-regulating kinase. The deduced protein contains 1,375 amino acids, and is most closely related to yeast SSK2 and SSK22, which are upstream regulators of yeast HOG1 MAPK. ASK1 expression complements a yeast mutant lacking functional SSK2 and SSK22. ASK1 also activates MKK3 (OMIM Ref. No. 602315), MKK4 (SEK1), and MKK6 (OMIM Ref. No. 601254). Overexpression of ASK1 induces apoptotic cell death, and ASK1 is activated in cells treated with tumor necrosis factor- $\alpha$  (TNF $\alpha$ ; 191160). Nishitoh et al. (1998) showed that ASK1 interacts with members of the TRAF family and is activated by TRAF2 (OMIM Ref. No. 601895) in the TNF-signaling pathway. After activation by TRAF2, ASK1 activates MKK4, which in turn activates JNK. Thus, ASK1 is a mediator of TRAF2-induced JNK activation. Animal model experiments lend further support to the function of MAP3K5. Using a forward genetic screen of *C. elegans* mutants, Kim et al. (2002) showed that viable worms lacking *esp2* and *esp8*, homologs of the mammalian MAP kinases SEK1 and ASK1, were highly susceptible to and died more rapidly from

both a gram-negative bacterium, *P. aeruginosa*, and a gram-positive organism, *E. faecalis*, than wildtype worms. RNA-interference and biochemical analyses likewise implicated the p38 MAP kinase homolog, *pmk1*, in susceptibility to these pathogens. Kim et al. (2002) concluded that MAP kinase signaling, which is also involved in plant pathogen resistance, is a conserved element in innate metazoan immunity to diverse pathogens.

[55080] It is appreciated that the abovementioned animal model for MAP3K5 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[55081] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55082] Kim, D. H.; Feinbaum, R.; Alloing, G.; Emerson, F. E.; Garsin, D. A.; Inoue, H.; Tanaka-Hino, M.; Hisamoto, N.; Matsumoto, K.; Tan, M.-W.; Ausubel, F. M. : A conserved p38 MAP kinase pathway in *Caenorhabditis elegans* innate immunity. *Science* 297: 623-626, 2002. ; and

[55083] Nishitoh, H.; Saitoh, M.; Mochida, Y.; Takeda, K.; Nakano, H.; Rothe, M.; Miyazono, K.; Ichijo, H. : ASK1 is essential for JNK/SAPK activation by TRAF2. *Molec. Cell* 2: 389-395,

1998.

[55084] Further studies establishing the function and utilities of MAP3K5 are found in John Hopkins OMIM database record ID 602448, and in cited publications numbered 5869–5871, 10126, 12537, 10348, 1035 and 6315 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prolactin Receptor (PRLR, Accession NM\_000949) is another VGAM1622 host target gene. PRLR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRLR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRLR BINDING SITE, designated SEQ ID:6650, to the nucleotide sequence of VGAM1622 RNA, herein designated VGAM RNA, also designated SEQ ID:4333.

[55085] Another function of VGAM1622 is therefore inhibition of Prolactin Receptor (PRLR, Accession NM\_000949), a gene which is a receptor for the anterior pituitary hormone prolactin. Accordingly, utilities of VGAM1622 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRLR. The function of PRLR and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM80.KIAA0310 (Accession XM\_088459) is another VGAM1622 host target gene. KIAA0310 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0310 BINDING SITE, designated SEQ ID:39711, to the nucleotide sequence of VGAM1622 RNA, herein designated VGAM RNA, also designated SEQ ID:4333.

[55086] Another function of VGAM1622 is therefore inhibition of KIAA0310 (Accession XM\_088459). Accordingly, utilities of VGAM1622 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0310. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1623 (VGAM1623) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[55087] VGAM1623 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1623 was detected is described hereinabove with reference to Figs. 1-8.

[55088] VGAM1623 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1623 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55089] VGAM1623 gene encodes a VGAM1623 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1623 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1623 precursor RNA is designated SEQ ID:1609, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1609 is located at position 83968 relative to the genome of Bovine Herpesvirus 4.

[55090] VGAM1623 precursor RNA folds onto itself, forming VGAM1623 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55091] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1623 folded precursor RNA into VGAM1623 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1623 RNA is designated SEQ ID:4334, and is provided hereinbelow with reference to the sequence listing part.

[55092] VGAM1623 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1623 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1623 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[55093] VGAM1623 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1623 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1623 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1623 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1623 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55094] The complementary binding of VGAM1623 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1623 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1623 host target RNA into VGAM1623 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55095] It is appreciated that VGAM1623 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1623 host target genes. The mRNA of each one of this plurality of VGAM1623 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1623 RNA, herein designated VGAM RNA, and which when bound by VGAM1623 RNA causes inhibition of translation of respective one or more VGAM1623 host target proteins.

[55096] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1623 gene, herein designated VGAM GENE, on one or more VGAM1623 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55097] It is yet further appreciated that a function of VGAM1623 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1623 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1623 correlate with, and may be deduced from, the identity of the host target genes which VGAM1623 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55098] Nucleotide sequences of the VGAM1623 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1623 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1623 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1623 are further  
described hereinbelow with reference to Table 1.

[55099] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1623 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1623 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[55100] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1623 gene, herein designated VGAM is  
inhibition of expression of VGAM1623 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1623 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1623  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[55101] FLJ23323 (Accession NM\_024654) is a VGAM1623 host  
target gene. FLJ23323 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ23323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23323 BINDING SITE, designated SEQ ID:23954, to the nucleotide sequence of VGAM1623 RNA, herein designated VGAM RNA, also designated SEQ ID:4334.

[55102] A function of VGAM1623 is therefore inhibition of FLJ23323 (Accession NM\_024654). Accordingly, utilities of VGAM1623 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23323. HSC3 (Accession NM\_145174) is another VGAM1623 host target gene. HSC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSC3 BINDING SITE, designated SEQ ID:29733, to the nucleotide sequence of VGAM1623 RNA, herein designated VGAM RNA, also designated SEQ ID:4334.

[55103] Another function of VGAM1623 is therefore inhibition of

HSC3 (Accession NM\_145174). Accordingly, utilities of VGAM1623 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSC3. LOC145623 (Accession XM\_096822) is another VGAM1623 host target gene. LOC145623 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145623, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145623 BINDING SITE, designated SEQ ID:40546, to the nucleotide sequence of VGAM1623 RNA, herein designated VGAM RNA, also designated SEQ ID:4334.

[55104] Another function of VGAM1623 is therefore inhibition of LOC145623 (Accession XM\_096822). Accordingly, utilities of VGAM1623 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145623. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1624 (VGAM1624) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes



is known in the art.

[55105] VGAM1624 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1624 was detected is described hereinabove with reference to Figs. 1–8.

[55106] VGAM1624 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1624 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55107] VGAM1624 gene encodes a VGAM1624 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1624 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1624 precursor RNA is designated SEQ ID:1610, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1610 is located at position 86638 relative to the genome of Bovine Herpesvirus 4.

[55108] VGAM1624 precursor RNA folds onto itself, forming VGAM1624 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55109] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1624 folded precursor RNA into VGAM1624 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1624 RNA is designated SEQ ID:4335, and is provided hereinbelow with reference to the sequence listing part.

[55110] VGAM1624 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1624 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1624 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[55111] VGAM1624 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1624 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1624 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1624 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1624 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[55112] The complementary binding of VGAM1624 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1624 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1624 host target RNA into VGAM1624 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55113] It is appreciated that VGAM1624 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1624 host target genes. The mRNA of each one of this plurality of VGAM1624 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1624 RNA, herein designated VGAM RNA, and which when bound by VGAM1624 RNA causes inhibition of translation of respective one or more VGAM1624 host target proteins.

[55114] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1624 gene, herein designated VGAM GENE, on one

or more VGAM1624 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55115] It is yet further appreciated that a function of VGAM1624 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1624 correlate with, and may be deduced from, the identity of the host target genes which VGAM1624 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55116] Nucleotide sequences of the VGAM1624 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1624 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1624 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1624 are further described hereinbelow with reference to Table 1.

[55117] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1624 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1624 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55118] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1624 gene, herein designated VGAM is inhibition of expression of VGAM1624 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1624 correlate with, and may be deduced from, the identity of the target genes which VGAM1624 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55119] B-cell CLL/lymphoma 2 (BCL2, Accession NM\_000633) is a

VGAM1624 host target gene. BCL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2 BINDING SITE, designated SEQ ID:6261, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also designated SEQ ID:4335.

[55120] A function of VGAM1624 is therefore inhibition of B-cell CLL/lymphoma 2 (BCL2, Accession NM\_000633). Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2. Cyclic Nucleotide Gated Channel Alpha 3 (CNCA3, Accession NM\_001298) is another VGAM1624 host target gene. CNCA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNCA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNCA3 BINDING SITE, designated SEQ ID:6977, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4335.

[55121] Another function of VGAM1624 is therefore inhibition of Cyclic Nucleotide Gated Channel Alpha 3 (CNGA3, Accession NM\_001298). Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNGA3. Potassium Voltage-gated Channel, Shaker-related Subfamily, Beta Member 2 (KCNAB2, Accession NM\_003636) is another VGAM1624 host target gene. KCNAB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNAB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNAB2 BINDING SITE, designated SEQ ID:9710, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also designated SEQ ID:4335.

[55122] Another function of VGAM1624 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Beta Member 2 (KCNAB2, Accession NM\_003636), a gene which is the beta subunit of shaker voltage-gated potassium channels. Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of diseases



and clinical conditions associated with KCNAB2. The function of KCNAB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM659. Steroidogenic Acute Regulatory Protein (STAR, Accession NM\_000349) is another VGAM1624 host target gene. STAR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAR BINDING SITE, designated SEQ ID:5903, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also designated SEQ ID:4335.

[55123] Another function of VGAM1624 is therefore inhibition of Steroidogenic Acute Regulatory Protein (STAR, Accession NM\_000349). Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAR. DnaJ (Hsp40) Homolog, Subfamily B, Member 5 (DNAJB5, Accession NM\_012266) is another VGAM1624 host target gene. DNAJB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

DNAJB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJB5 BINDING SITE, designated SEQ ID:14586, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also designated SEQ ID:4335.

[55124] Another function of VGAM1624 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily B, Member 5 (DNAJB5, Accession NM\_012266). Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJB5. Mitogen-activated Protein Kinase Kinase Kinase 2 (MAP3K2, Accession NM\_006609) is another VGAM1624 host target gene. MAP3K2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K2 BINDING SITE, designated SEQ ID:13386, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also designated SEQ ID:4335.

[55125] Another function of VGAM1624 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 2 (MAP3K2, Accession NM\_006609). Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K2. LOC148809 (Accession XM\_086325) is another VGAM1624 host target gene. LOC148809 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148809, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148809 BINDING SITE, designated SEQ ID:38596, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also designated SEQ ID:4335.

[55126] Another function of VGAM1624 is therefore inhibition of LOC148809 (Accession XM\_086325). Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148809. LOC149372 (Accession XM\_086509) is another VGAM1624 host target gene. LOC149372 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149372, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149372 BINDING SITE, designated SEQ ID:38726, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also designated SEQ ID:4335.

[55127] Another function of VGAM1624 is therefore inhibition of LOC149372 (Accession XM\_086509). Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149372. LOC158428 (Accession XM\_047249) is another VGAM1624 host target gene. LOC158428 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158428, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158428 BINDING SITE, designated SEQ ID:34920, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also designated SEQ ID:4335.

[55128] Another function of VGAM1624 is therefore inhibition of LOC158428 (Accession XM\_047249). Accordingly, utilities of VGAM1624 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC158428. LOC169026 (Accession XM\_095471) is another VGAM1624 host target gene. LOC169026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169026 BINDING SITE, designated SEQ ID:40267, to the nucleotide sequence of VGAM1624 RNA, herein designated VGAM RNA, also designated SEQ ID:4335.

[55129] Another function of VGAM1624 is therefore inhibition of LOC169026 (Accession XM\_095471). Accordingly, utilities of VGAM1624 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169026. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1625 (VGAM1625) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55130] VGAM1625 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1625 was detected is described hereinabove with reference to Figs. 1–8.

[55131] VGAM1625 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1625 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55132] VGAM1625 gene encodes a VGAM1625 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1625 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1625 precursor RNA is designated SEQ ID:1611, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1611 is located at position 86511 relative to the genome of Bovine Herpesvirus 4.

[55133] VGAM1625 precursor RNA folds onto itself, forming VGAM1625 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55134] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1625 folded precursor RNA into VGAM1625 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1625 RNA is designated SEQ ID:4336, and is provided hereinbelow with reference to the sequence listing part.

[55135] VGAM1625 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1625 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1625 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55136] VGAM1625 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1625 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1625 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1625 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1625 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55137] The complementary binding of VGAM1625 RNA, herein



designated VGAM RNA, to host target binding sites on VGAM1625 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1625 host target RNA into VGAM1625 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55138] It is appreciated that VGAM1625 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1625 host target genes. The mRNA of each one of this plurality of VGAM1625 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1625 RNA, herein designated VGAM RNA, and which when bound by VGAM1625 RNA causes inhibition of translation of respective one or more VGAM1625 host target proteins.

[55139] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1625 gene, herein designated VGAM GENE, on one or more VGAM1625 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55140] It is yet further appreciated that a function of VGAM1625 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1625 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1625 correlate with, and may be deduced from, the identity of the host target genes which VGAM1625 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55141] Nucleotide sequences of the VGAM1625 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1625 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1625 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1625 are further described hereinbelow with reference to Table 1.

[55142] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1625 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1625 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55143] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1625 gene, herein designated VGAM is inhibition of expression of VGAM1625 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1625 correlate with, and may be deduced from, the identity of the target genes which VGAM1625 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55144] Synaptotagmin XIII (SYT13, Accession XM\_167880) is a VGAM1625 host target gene. SYT13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by SYT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYT13 BINDING SITE, designated SEQ ID:44885, to the nucleotide sequence of VGAM1625 RNA, herein designated VGAM RNA, also designated SEQ ID:4336.

[55145] A function of VGAM1625 is therefore inhibition of Synaptotagmin XIII (SYT13, Accession XM\_167880). Accordingly, utilities of VGAM1625 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYT13. LOC148545 (Accession XM\_086226) is another VGAM1625 host target gene. LOC148545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148545 BINDING SITE, designated SEQ ID:38552, to the nucleotide sequence of VGAM1625 RNA, herein designated VGAM RNA, also designated SEQ ID:4336.

[55146] Another function of VGAM1625 is therefore inhibition of LOC148545 (Accession XM\_086226). Accordingly, utilities

of VGAM1625 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148545. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1626 (VGAM1626) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55147] VGAM1626 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1626 was detected is described hereinabove with reference to Figs. 1–8.

[55148] VGAM1626 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1626 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55149] VGAM1626 gene encodes a VGAM1626 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1626 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu–

cleotide sequence of VGAM1626 precursor RNA is designated SEQ ID:1612, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1612 is located at position 80653 relative to the genome of Bovine Herpesvirus 4.

- [55150] VGAM1626 precursor RNA folds onto itself, forming VGAM1626 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [55151] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1626 folded precursor RNA into VGAM1626 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1626 RNA is designated SEQ ID:4337, and

is provided hereinbelow with reference to the sequence listing part.

[55152] VGAM1626 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1626 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1626 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[55153] VGAM1626 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1626 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1626 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1626 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1626 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55154] The complementary binding of VGAM1626 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1626 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1626 host target RNA into VGAM1626 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55155] It is appreciated that VGAM1626 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1626 host target genes. The mRNA of each one of this plurality of VGAM1626 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–



plementary to VGAM1626 RNA, herein designated VGAM RNA, and which when bound by VGAM1626 RNA causes inhibition of translation of respective one or more VGAM1626 host target proteins.

[55156] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1626 gene, herein designated VGAM GENE, on one or more VGAM1626 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55157] It is yet further appreciated that a function of VGAM1626 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1626 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1626 correlate with, and may be deduced from, the identity of the host target genes which VGAM1626 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55158] Nucleotide sequences of the VGAM1626 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1626 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1626 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1626 are further described hereinbelow with reference to Table 1.

[55159] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1626 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1626 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55160] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1626 gene, herein designated VGAM is inhibition of expression of VGAM1626 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1626 correlate with, and may be deduced from, the identity of the target genes which VGAM1626 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55161] Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM\_052988) is a VGAM1626 host target gene. CDK10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDK10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK10 BINDING SITE, designated SEQ ID:27554, to the nucleotide sequence of VGAM1626 RNA, herein designated VGAM RNA, also designated SEQ ID:4337.

[55162] A function of VGAM1626 is therefore inhibition of Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM\_052988), a gene which plays a pivotal role in the regulation of the eukaryotic cell cycle. Accordingly, utilities of VGAM1626 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CDK10. The function of CDK10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM193. Endoglin (Osler–Rendu–Weber syndrome 1) (ENG, Accession NM\_000118) is another VGAM1626 host target gene. ENG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ENG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENG BINDING SITE, designated SEQ ID:5594, to the nucleotide sequence of VGAM1626 RNA, herein designated VGAM RNA, also designated SEQ ID:4337.

[55163] Another function of VGAM1626 is therefore inhibition of Endoglin (Osler–Rendu–Weber syndrome 1) (ENG, Accession NM\_000118). Accordingly, utilities of VGAM1626 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENG. FLJ21438 (Accession XM\_029084) is another VGAM1626 host target gene. FLJ21438 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21438, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21438 BINDING SITE, designated SEQ ID:30845, to the nucleotide sequence of VGAM1626 RNA, herein designated VGAM RNA, also designated SEQ ID:4337.

[55164] Another function of VGAM1626 is therefore inhibition of FLJ21438 (Accession XM\_029084). Accordingly, utilities of VGAM1626 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21438. KIAA1610 (Accession XM\_040622) is another VGAM1626 host target gene. KIAA1610 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1610, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1610 BINDING SITE, designated SEQ ID:33339, to the nucleotide sequence of VGAM1626 RNA, herein designated VGAM RNA, also designated SEQ ID:4337.

[55165] Another function of VGAM1626 is therefore inhibition of KIAA1610 (Accession XM\_040622). Accordingly, utilities of VGAM1626 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1610. LOC221477 (Accession XM\_166397) is another VGAM1626 host target gene. LOC221477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221477 BINDING SITE, designated SEQ ID:44253, to the nucleotide sequence of VGAM1626 RNA, herein designated VGAM RNA, also designated SEQ ID:4337.

[55166] Another function of VGAM1626 is therefore inhibition of LOC221477 (Accession XM\_166397). Accordingly, utilities of VGAM1626 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221477. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1627 (VGAM1627) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55167] VGAM1627 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1627 was detected is described hereinabove with reference to Figs. 1–8.

[55168] VGAM1627 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1627 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55169] VGAM1627 gene encodes a VGAM1627 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1627 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1627 precursor RNA is designated SEQ ID:1613, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1613 is located at position 80799 relative to the genome of Bovine Herpesvirus 4.

[55170] VGAM1627 precursor RNA folds onto itself, forming VGAM1627 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55171] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1627 folded precursor RNA into VGAM1627 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1627 RNA is designated SEQ ID:4338, and is provided hereinbelow with reference to the sequence listing part.

[55172] VGAM1627 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1627 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1627 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.



[55173] VGAM1627 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1627 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1627 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1627 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1627 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55174] The complementary binding of VGAM1627 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1627 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1627 host target RNA into VGAM1627 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55175] It is appreciated that VGAM1627 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1627 host target genes. The mRNA of each one of this plurality of VGAM1627 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1627 RNA, herein designated VGAM RNA, and which when bound by VGAM1627 RNA causes inhibition of translation of respective one or more VGAM1627 host target proteins.

[55176] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1627 gene, herein designated VGAM GENE, on one or more VGAM1627 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55177] It is yet further appreciated that a function of VGAM1627 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1627 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1627 correlate with, and may be deduced from, the identity of the host target genes which VGAM1627 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55178] Nucleotide sequences of the VGAM1627 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1627 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1627 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1627 are further described hereinbelow with reference to Table 1.

[55179] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1627 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1627 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55180] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1627 gene, herein designated VGAM is inhibition of expression of VGAM1627 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1627 correlate with, and may be deduced from, the identity of the target genes which VGAM1627 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55181] LNK (Accession NM\_005475) is a VGAM1627 host target gene. LNK BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

LNK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LNK BINDING SITE, designated SEQ ID:11970, to the nucleotide sequence of VGAM1627 RNA, herein designated VGAM RNA, also designated SEQ ID:4338.

[55182] A function of VGAM1627 is therefore inhibition of LNK (Accession NM\_005475), a gene which links T-cell receptor activation signal to phospholipase c-gamma-1, grb-2 and phosphatidylinositol 3-kinase (by similarity). Accordingly, utilities of VGAM1627 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LNK. The function of LNK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM115. Myosin IIIB (MYO3B, Accession NM\_138995) is another VGAM1627 host target gene. MYO3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYO3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO3B BINDING SITE, designated SEQ

ID:29094, to the nucleotide sequence of VGAM1627 RNA, herein designated VGAM RNA, also designated SEQ ID:4338.

[55183] Another function of VGAM1627 is therefore inhibition of Myosin IIIB (MYO3B, Accession NM\_138995). Accordingly, utilities of VGAM1627 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO3B. LOC219920 (Accession XM\_167787) is another VGAM1627 host target gene. LOC219920 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219920 BINDING SITE, designated SEQ ID:44802, to the nucleotide sequence of VGAM1627 RNA, herein designated VGAM RNA, also designated SEQ ID:4338.

[55184] Another function of VGAM1627 is therefore inhibition of LOC219920 (Accession XM\_167787). Accordingly, utilities of VGAM1627 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219920. LOC220279 (Accession XM\_169083) is another VGAM1627 host target gene. LOC220279 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220279, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220279 BINDING SITE, designated SEQ ID:45288, to the nucleotide sequence of VGAM1627 RNA, herein designated VGAM RNA, also designated SEQ ID:4338.

[55185] Another function of VGAM1627 is therefore inhibition of LOC220279 (Accession XM\_169083). Accordingly, utilities of VGAM1627 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220279. LOC255826 (Accession XM\_173938) is another VGAM1627 host target gene. LOC255826 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255826 BINDING SITE, designated SEQ ID:46569, to the nucleotide sequence of VGAM1627 RNA, herein designated VGAM RNA, also designated SEQ ID:4338.

[55186] Another function of VGAM1627 is therefore inhibition of

LOC255826 (Accession XM\_173938). Accordingly, utilities of VGAM1627 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255826. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1628 (VGAM1628) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55187] VGAM1628 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1628 was detected is described hereinabove with reference to Figs. 1-8.

[55188] VGAM1628 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1628 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55189] VGAM1628 gene encodes a VGAM1628 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1628 precursor RNA does not encode a protein. A



nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1628 precursor RNA is designated SEQ ID:1614, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1614 is located at position 83406 relative to the genome of Bovine Herpesvirus 4.

- [55190] VGAM1628 precursor RNA folds onto itself, forming VGAM1628 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [55191] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1628 folded precursor RNA into VGAM1628 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide se-

quence of VGAM1628 RNA is designated SEQ ID:4339, and is provided hereinbelow with reference to the sequence listing part.

[55192] VGAM1628 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1628 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1628 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55193] VGAM1628 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1628 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1628 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1628 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1628 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[55194] The complementary binding of VGAM1628 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1628 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1628 host target RNA into VGAM1628 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55195] It is appreciated that VGAM1628 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1628 host target genes. The mRNA of each one of this plurality of VGAM1628 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1628 RNA, herein designated VGAM RNA, and which when bound by VGAM1628 RNA causes inhibition of translation of respective one or more VGAM1628 host target proteins.

[55196] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1628 gene, herein designated VGAM GENE, on one or more VGAM1628 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55197] It is yet further appreciated that a function of VGAM1628

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1628 correlate with, and may be deduced from, the identity of the host target genes which VGAM1628 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55198] Nucleotide sequences of the VGAM1628 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1628 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1628 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1628 are further described hereinbelow with reference to Table 1.

[55199] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1628 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1628 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55200] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1628 gene, herein designated VGAM is inhibition of expression of VGAM1628 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1628 correlate with, and may be deduced from, the identity of the target genes which VGAM1628 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55201] Down-regulator of Transcription 1, TBP-binding (negative cofactor 2) (DR1, Accession XM\_002015) is a VGAM1628 host target gene. DR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DR1 BINDING SITE, designated SEQ ID:29858, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55202] A function of VGAM1628 is therefore inhibition of Down-regulator of Transcription 1, TBP-binding (negative cofactor 2) (DR1, Accession XM\_002015), a gene which influences functional repression of both activated and basal

transcription of class ii genes. Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DR1. The function of DR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM711. Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession NM\_000134) is another VGAM1628 host target gene. FABP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FABP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FABP2 BINDING SITE, designated SEQ ID:5625, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55203] Another function of VGAM1628 is therefore inhibition of Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession NM\_000134), a gene which may have a role in dietary fat uptake or processing. Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FABP2. The func-

tion of FABP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM951. Lactate Dehydrogenase B (LDHB, Accession NM\_002300) is another VGAM1628 host target gene. LDHB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LDHB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDHB BINDING SITE, designated SEQ ID:8088, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55204] Another function of VGAM1628 is therefore inhibition of Lactate Dehydrogenase B (LDHB, Accession NM\_002300), a gene which causes dehydrogenation of lactate. Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDHB. The function of LDHB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM273. AUT-like 1, Cysteine Endopeptidase (*S. cerevisiae*) (AUTL1, Accession



NM\_032852) is another VGAM1628 host target gene.

AUTL1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by AUTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AUTL1 BINDING SITE, designated SEQ ID:26647, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55205] Another function of VGAM1628 is therefore inhibition of AUT-like 1, Cysteine Endopeptidase (*S. cerevisiae*) (AUTL1, Accession NM\_032852). Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AUTL1. UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 1 (B3GALT1, Accession NM\_020981) is another VGAM1628 host target gene. B3GALT1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by B3GALT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT1

BINDING SITE, designated SEQ ID:21971, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55206] Another function of VGAM1628 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 1 (B3GALT1, Accession NM\_020981). Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT1. GNB4 (Accession NM\_021629) is another VGAM1628 host target gene. GNB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNB4 BINDING SITE, designated SEQ ID:22267, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55207] Another function of VGAM1628 is therefore inhibition of GNB4 (Accession NM\_021629). Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNB4. OBTP (Accession NM\_017601) is another VGAM1628 host

target gene. OBTP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by OBTP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OBTP BINDING SITE, designated SEQ ID:19081, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55208] Another function of VGAM1628 is therefore inhibition of OBTP (Accession NM\_017601). Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OBTP. LOC157663 (Accession XM\_088354) is another VGAM1628 host target gene. LOC157663 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC157663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157663 BINDING SITE, designated SEQ ID:39637, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55209] Another function of VGAM1628 is therefore inhibition of LOC157663 (Accession XM\_088354). Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157663. LOC199926 (Accession XM\_117157) is another VGAM1628 host target gene. LOC199926 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199926, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199926 BINDING SITE, designated SEQ ID:43262, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55210] Another function of VGAM1628 is therefore inhibition of LOC199926 (Accession XM\_117157). Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199926. LOC202316 (Accession XM\_117380) is another VGAM1628 host target gene. LOC202316 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202316, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202316 BINDING SITE, designated SEQ ID:43427, to the nucleotide sequence of VGAM1628 RNA, herein designated VGAM RNA, also designated SEQ ID:4339.

[55211] Another function of VGAM1628 is therefore inhibition of LOC202316 (Accession XM\_117380). Accordingly, utilities of VGAM1628 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202316. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1629 (VGAM1629) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55212] VGAM1629 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1629 was detected is described hereinabove with reference to Figs. 1-8.

[55213] VGAM1629 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1629 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[55214] VGAM1629 gene encodes a VGAM1629 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1629 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1629 precursor RNA is designated SEQ ID:1615, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1615 is located at position 88808 relative to the genome of Bovine Herpesvirus 4.

[55215] VGAM1629 precursor RNA folds onto itself, forming VGAM1629 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55216] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1629 folded precursor RNA into VGAM1629

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1629 RNA is designated SEQ ID:4340, and is provided hereinbelow with reference to the sequence listing part.

[55217] VGAM1629 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1629 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1629 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55218] VGAM1629 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1629 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1629 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1629 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1629 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55219] The complementary binding of VGAM1629 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1629 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1629 host target RNA into VGAM1629 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM



host target protein is therefore outlined by a broken line.

[55220] It is appreciated that VGAM1629 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1629 host target genes. The mRNA of each one of this plurality of VGAM1629 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1629 RNA, herein designated VGAM RNA, and which when bound by VGAM1629 RNA causes inhibition of translation of respective one or more VGAM1629 host target proteins.

[55221] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1629 gene, herein designated VGAM GENE, on one or more VGAM1629 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55222] It is yet further appreciated that a function of VGAM1629 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1629 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1629 correlate with, and may be deduced from, the identity of the host target genes which VGAM1629 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55223] Nucleotide sequences of the VGAM1629 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1629 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1629 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1629 are further described hereinbelow with reference to Table 1.

[55224] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1629 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1629 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55225] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1629 gene, herein designated VGAM is inhibition of expression of VGAM1629 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1629 correlate with, and may be deduced from, the identity of the target genes which VGAM1629 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55226] DnaJ (Hsp40) Homolog, Subfamily B, Member 5 (DNAJB5, Accession NM\_012266) is a VGAM1629 host target gene. DNAJB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJB5 BINDING SITE, designated SEQ ID:14587, to the nucleotide sequence of VGAM1629 RNA,

herein designated VGAM RNA, also designated SEQ ID:4340.

[55227] A function of VGAM1629 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily B, Member 5 (DNAJB5, Accession NM\_012266). Accordingly, utilities of VGAM1629 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJB5. KIAA1001 (Accession NM\_014960) is another VGAM1629 host target gene. KIAA1001 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1001 BINDING SITE, designated SEQ ID:17326, to the nucleotide sequence of VGAM1629 RNA, herein designated VGAM RNA, also designated SEQ ID:4340.

[55228] Another function of VGAM1629 is therefore inhibition of KIAA1001 (Accession NM\_014960). Accordingly, utilities of VGAM1629 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1001. Kinase Suppressor of Ras (KSR, Accession XM\_034172) is another VGAM1629 host target gene. KSR

BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KSR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KSR BINDING SITE, designated SEQ ID:32020, to the nucleotide sequence of VGAM1629 RNA, herein designated VGAM RNA, also designated SEQ ID:4340.

[55229] Another function of VGAM1629 is therefore inhibition of Kinase Suppressor of Ras (KSR, Accession XM\_034172). Accordingly, utilities of VGAM1629 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KSR. PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM\_028335) is another VGAM1629 host target gene. PRPF8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRPF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPF8 BINDING SITE, designated SEQ ID:30679, to the nucleotide sequence of VGAM1629 RNA, herein designated VGAM RNA, also designated SEQ ID:4340.

[55230] Another function of VGAM1629 is therefore inhibition of PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM\_028335). Accordingly, utilities of VGAM1629 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRPF8. SR-BP1 (Accession NM\_005866) is another VGAM1629 host target gene. SR-BP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SR-BP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SR-BP1 BINDING SITE, designated SEQ ID:12484, to the nucleotide sequence of VGAM1629 RNA, herein designated VGAM RNA, also designated SEQ ID:4340.

[55231] Another function of VGAM1629 is therefore inhibition of SR-BP1 (Accession NM\_005866). Accordingly, utilities of VGAM1629 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SR-BP1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1630 (VGAM1630) viral gene, which modulates expression

of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55232] VGAM1630 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1630 was detected is described hereinabove with reference to Figs. 1–8.

[55233] VGAM1630 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1630 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55234] VGAM1630 gene encodes a VGAM1630 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1630 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1630 precursor RNA is designated SEQ ID:1616, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1616 is located at position 84159 relative to the genome of Bovine Herpesvirus 4.

[55235] VGAM1630 precursor RNA folds onto itself, forming VGAM1630 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55236] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1630 folded precursor RNA into VGAM1630 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 63%) nucleotide sequence of VGAM1630 RNA is designated SEQ ID:4341, and is provided hereinbelow with reference to the sequence listing part.

[55237] VGAM1630 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1630 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1630 host target RNA comprises three regions, as is typical of mRNA of a pro-



tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55238] VGAM1630 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1630 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1630 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1630 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1630 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55239] The complementary binding of VGAM1630 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1630 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1630 host target RNA into VGAM1630 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55240] It is appreciated that VGAM1630 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1630 host target genes. The mRNA of each one of this plurality of VGAM1630 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1630 RNA, herein designated VGAM RNA, and which when bound by VGAM1630 RNA causes inhibition of translation of respective one or more VGAM1630 host target proteins.

[55241] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1630 gene, herein designated VGAM GENE, on one or more VGAM1630 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55242] It is yet further appreciated that a function of VGAM1630 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1630 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1630 correlate with, and may be deduced from, the identity of the host target genes which VGAM1630 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[55243] Nucleotide sequences of the VGAM1630 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1630 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1630 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1630 are further described hereinbelow with reference to Table 1.

[55244] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1630 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1630 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55245] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1630 gene, herein designated VGAM is inhibition of expression of VGAM1630 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1630 correlate with, and may be deduced from, the identity of the target genes which VGAM1630 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55246] Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession NM\_000134) is a VGAM1630 host target gene. FABP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FABP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FABP2 BINDING SITE, designated SEQ ID:5626, to the nucleotide sequence of VGAM1630 RNA, herein designated VGAM RNA, also designated SEQ ID:4341.

[55247] A function of VGAM1630 is therefore inhibition of Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession NM\_000134), a gene which may have a role in dietary fat uptake or processing. Accordingly, utilities of VGAM1630 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FABP2. The function of FABP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM951. Protein Kinase, AMP-activated, Alpha 2 Catalytic Subunit (PRKAA2, Accession NM\_006252) is another VGAM1630 host target gene. PRKAA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PRKAA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAA2 BINDING SITE, designated SEQ ID:12929, to the nucleotide sequence of VGAM1630 RNA, herein designated VGAM RNA, also designated SEQ ID:4341.

[55248] Another function of VGAM1630 is therefore inhibition of Protein Kinase, AMP-activated, Alpha 2 Catalytic Subunit (PRKAA2, Accession NM\_006252), a gene which are responsible for the regulation of fatty acid synthesis by phosphorylation of acetyl-coa carboxylase. Accordingly, utilities of VGAM1630 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAA2. The function of PRKAA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1544. G-protein Coupled Receptor 88 (GPR88, Accession NM\_022049) is another VGAM1630 host target gene. GPR88 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR88, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR88 BINDING SITE, designated SEQ ID:22571, to the nucleotide sequence of VGAM1630 RNA, herein designated VGAM RNA, also designated SEQ ID:4341.

[55249] Another function of VGAM1630 is therefore inhibition of G-protein Coupled Receptor 88 (GPR88, Accession NM\_022049). Accordingly, utilities of VGAM1630 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR88. LOC148946 (Accession XM\_097557) is another VGAM1630 host target gene. LOC148946 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148946, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148946 BINDING SITE, designated SEQ ID:40937, to the nucleotide sequence of VGAM1630 RNA, herein designated VGAM RNA, also designated SEQ ID:4341.

[55250] Another function of VGAM1630 is therefore inhibition of LOC148946 (Accession XM\_097557). Accordingly, utilities of VGAM1630 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC148946. LOC90750 (Accession XM\_033868) is another VGAM1630 host target gene. LOC90750 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90750 BINDING SITE, designated SEQ ID:31966, to the nucleotide sequence of VGAM1630 RNA, herein designated VGAM RNA, also designated SEQ ID:4341.

[55251] Another function of VGAM1630 is therefore inhibition of LOC90750 (Accession XM\_033868). Accordingly, utilities of VGAM1630 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90750. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1631 (VGAM1631) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55252] VGAM1631 is a novel bioinformatically detected regula-



tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1631 was detected is described hereinabove with reference to Figs. 1–8.

[55253] VGAM1631 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1631 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55254] VGAM1631 gene encodes a VGAM1631 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1631 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1631 precursor RNA is designated SEQ ID:1617, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1617 is located at position 90442 relative to the genome of Bovine Herpesvirus 4.

[55255] VGAM1631 precursor RNA folds onto itself, forming VGAM1631 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55256] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1631 folded precursor RNA into VGAM1631 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1631 RNA is designated SEQ ID:4342, and is provided hereinbelow with reference to the sequence listing part.

[55257] VGAM1631 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1631 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1631 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55258] VGAM1631 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1631 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1631 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1631 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1631 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55259] The complementary binding of VGAM1631 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1631 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1631 host target RNA into VGAM1631 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55260] It is appreciated that VGAM1631 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1631 host target genes. The mRNA of each one of this plurality of VGAM1631 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1631 RNA, herein designated VGAM RNA, and which when bound by VGAM1631 RNA causes inhibition of translation of respective one or more VGAM1631 host target proteins.

[55261] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1631 gene, herein designated VGAM GENE, on one or more VGAM1631 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55262] It is yet further appreciated that a function of VGAM1631 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1631 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1631 correlate with, and may be deduced from, the identity of the host target genes which VGAM1631 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55263] Nucleotide sequences of the VGAM1631 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1631 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1631 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1631 are further described hereinbelow with reference to Table 1.

[55264] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1631 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1631 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55265] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1631 gene, herein designated VGAM is inhibition of expression of VGAM1631 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1631 correlate with, and may be deduced from, the identity of the target genes which VGAM1631 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55266] Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542) is a VGAM1631 host target gene. HGF BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45221, to the nucleotide sequence of VGAM1631 RNA, herein designated VGAM RNA, also designated SEQ ID:4342.

[55267] A function of VGAM1631 is therefore inhibition of Hepatocyte Growth Factor (hepatopoietin A; scatter factor) (HGF, Accession XM\_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM1631 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. Muscleblind-like (Drosophila) (MBNL, Accession NM\_021038) is another VGAM1631 host target gene. MBNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of MBNL BINDING SITE, designated SEQ ID:22028, to the nucleotide sequence of VGAM1631 RNA, herein designated VGAM RNA, also designated SEQ ID:4342.

[55268] Another function of VGAM1631 is therefore inhibition of Muscleblind-like (Drosophila) (MBNL, Accession NM\_021038), a gene which binds to cug triplet repeat expansion dsrna (by similarity). Accordingly, utilities of VGAM1631 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBNL. The function of MBNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Protein Phosphatase 3 (formerly 2B), Regulatory Subunit B, 19kDa, Alpha Isoform (calcineurin B, type I) (PPP3R1, Accession XM\_084103) is another VGAM1631 host target gene. PPP3R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP3R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP3R1 BINDING SITE, designated SEQ ID:37530, to the nucleotide sequence of



VGAM1631 RNA, herein designated VGAM RNA, also designated SEQ ID:4342.

[55269] Another function of VGAM1631 is therefore inhibition of Protein Phosphatase 3 (formerly 2B), Regulatory Subunit B, 19kDa, Alpha Isoform (calcineurin B, type I) (PPP3R1, Accession XM\_084103), a gene which is a regulatory subunit of calcineurin, a calcium-dependent, calmodulin stimulated protein phosphatase 3. Accordingly, utilities of VGAM1631 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP3R1. The function of PPP3R1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM323.LOC116068 (Accession XM\_057302) is another VGAM1631 host target gene. LOC116068 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116068, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116068 BINDING SITE, designated SEQ ID:36500, to the nucleotide sequence of VGAM1631 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4342.

[55270] Another function of VGAM1631 is therefore inhibition of LOC116068 (Accession XM\_057302). Accordingly, utilities of VGAM1631 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116068. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1632 (VGAM1632) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55271] VGAM1632 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1632 was detected is described hereinabove with reference to Figs. 1–8.

[55272] VGAM1632 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1632 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55273] VGAM1632 gene encodes a VGAM1632 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1632 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1632 precursor RNA is designated SEQ ID:1618, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1618 is located at position 85979 relative to the genome of Bovine Herpesvirus 4.

- [55274] VGAM1632 precursor RNA folds onto itself, forming VGAM1632 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [55275] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1632 folded precursor RNA into VGAM1632 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1632 RNA is designated SEQ ID:4343, and is provided hereinbelow with reference to the sequence listing part.

[55276] VGAM1632 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1632 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1632 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55277] VGAM1632 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1632 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1632 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1632 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1632 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55278] The complementary binding of VGAM1632 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1632 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1632 host target RNA into VGAM1632 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55279] It is appreciated that VGAM1632 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1632 host target genes. The mRNA of

each one of this plurality of VGAM1632 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1632 RNA, herein designated VGAM RNA, and which when bound by VGAM1632 RNA causes inhibition of translation of respective one or more VGAM1632 host target proteins.

[55280] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1632 gene, herein designated VGAM GENE, on one or more VGAM1632 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[55281] It is yet further appreciated that a function of VGAM1632 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1632 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1632 correlate with, and may be deduced from, the identity of the host target genes which VGAM1632 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55282] Nucleotide sequences of the VGAM1632 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1632 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1632 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1632 are further described hereinbelow with reference to Table 1.

[55283] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1632 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1632 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55284] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1632 gene, herein designated VGAM is inhibition of expression of VGAM1632 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1632 correlate with, and may be deduced from, the identity of the target genes which VGAM1632 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55285] Rho GTPase Activating Protein 6 (ARHGAP6, Accession NM\_001174) is a VGAM1632 host target gene. ARHGAP6 BINDING SITE1 and ARHGAP6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ARHGAP6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP6 BINDING SITE1 and ARHGAP6 BINDING SITE2, designated SEQ ID:6838 and SEQ ID:15082 respectively, to the nucleotide sequence of VGAM1632 RNA, herein designated VGAM RNA, also designated SEQ ID:4343.

[55286] A function of VGAM1632 is therefore inhibition of Rho



GTPase Activating Protein 6 (ARHGAP6, Accession NM\_001174), a gene which activates the rho-type GTPases by converting them to an inactive GTP-bound state. Accordingly, utilities of VGAM1632 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP6. The function of ARHGAP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.FLJ10743 (Accession NM\_018201) is another VGAM1632 host target gene. FLJ10743 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10743 BINDING SITE, designated SEQ ID:20075, to the nucleotide sequence of VGAM1632 RNA, herein designated VGAM RNA, also designated SEQ ID:4343.

[55287] Another function of VGAM1632 is therefore inhibition of FLJ10743 (Accession NM\_018201). Accordingly, utilities of VGAM1632 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10743. Homocysteine-inducible, Endoplasmic Reticulum Stress-inducible, Ubiquitin-like Domain Member 1 (HERPUD1, Accession NM\_014685) is another VGAM1632 host target gene. HERPUD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HERPUD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HERPUD1 BINDING SITE, designated SEQ ID:16186, to the nucleotide sequence of VGAM1632 RNA, herein designated VGAM RNA, also designated SEQ ID:4343.

[55288] Another function of VGAM1632 is therefore inhibition of Homocysteine-inducible, Endoplasmic Reticulum Stress-inducible, Ubiquitin-like Domain Member 1 (HERPUD1, Accession NM\_014685). Accordingly, utilities of VGAM1632 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HERPUD1. Zinc Finger Protein 95 Homolog (mouse) (ZFP95, Accession NM\_014569) is another VGAM1632 host target gene. ZFP95 BINDING SITE1 and ZFP95 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ZFP95, corresponding to HOST TAR-

GET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP95 BINDING SITE1 and ZFP95 BINDING SITE2, designated SEQ ID:15920 and SEQ ID:29710 respectively, to the nucleotide sequence of VGAM1632 RNA, herein designated VGAM RNA, also designated SEQ ID:4343.

[55289] Another function of VGAM1632 is therefore inhibition of Zinc Finger Protein 95 Homolog (mouse) (ZFP95, Accession NM\_014569). Accordingly, utilities of VGAM1632 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP95. LOC255030 (Accession XM\_173197) is another VGAM1632 host target gene. LOC255030 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255030, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255030 BINDING SITE, designated SEQ ID:46439, to the nucleotide sequence of VGAM1632 RNA, herein designated VGAM RNA, also designated SEQ ID:4343.

[55290] Another function of VGAM1632 is therefore inhibition of

LOC255030 (Accession XM\_173197). Accordingly, utilities of VGAM1632 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255030. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1633 (VGAM1633) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55291] VGAM1633 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1633 was detected is described hereinabove with reference to Figs. 1-8.

[55292] VGAM1633 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1633 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55293] VGAM1633 gene encodes a VGAM1633 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1633 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1633 precursor RNA is designated SEQ ID:1619, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1619 is located at position 85246 relative to the genome of Bovine Herpesvirus 4.

- [55294] VGAM1633 precursor RNA folds onto itself, forming VGAM1633 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [55295] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1633 folded precursor RNA into VGAM1633 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide se-

quence of VGAM1633 RNA is designated SEQ ID:4344, and is provided hereinbelow with reference to the sequence listing part.

[55296] VGAM1633 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1633 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1633 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55297] VGAM1633 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1633 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1633 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1633 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1633 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55298] The complementary binding of VGAM1633 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1633 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1633 host target RNA into VGAM1633 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55299] It is appreciated that VGAM1633 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1633 host target genes. The mRNA of each one of this plurality of VGAM1633 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1633 RNA, herein designated VGAM RNA, and which when bound by VGAM1633 RNA causes inhibition of translation of respective one or more VGAM1633 host target proteins.

[55300] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1633 gene, herein designated VGAM GENE, on one or more VGAM1633 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55301] It is yet further appreciated that a function of VGAM1633



is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1633 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1633 correlate with, and may be deduced from, the identity of the host target genes which VGAM1633 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55302] Nucleotide sequences of the VGAM1633 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1633 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1633 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1633 are further described hereinbelow with reference to Table 1.

[55303] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1633 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1633 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55304] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1633 gene, herein designated VGAM is inhibition of expression of VGAM1633 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1633 correlate with, and may be deduced from, the identity of the target genes which VGAM1633 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55305] RAB Interacting Factor (RABIF, Accession NM\_002871) is a VGAM1633 host target gene. RABIF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RABIF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RABIF BINDING SITE, designated SEQ ID:8779, to the nucleotide sequence of VGAM1633 RNA, herein designated VGAM RNA, also designated SEQ ID:4344.

[55306] A function of VGAM1633 is therefore inhibition of RAB Interacting Factor (RABIF, Accession NM\_002871), a gene which is involved in the regulation of intracellular vesicular transport. Accordingly, utilities of VGAM1633 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with RABIF. The function of RABIF has been established by previous studies. The Sec4/Rab-related small GTP-binding proteins are involved in the regulation of intracellular vesicular transport. Mss4 stimulates GTP-GDP exchange in Sec4 and Rab and binds to a subset of genetically related Rab proteins. Yu and Schreiber (1995) cloned a human MSS4 cDNA. The gene encodes a 123-amino acid polypeptide that requires zinc for stability. Muller-Pillasch et al. (1997) showed by Northern blot analysis that MSS4 is expressed as 3 differently sized mRNAs, probably due to alternative polyadenylation signals. The transcripts are present at barely detectable levels in healthy pancreas, but at much higher levels in pancreatic and other cancer tissues. Muller-Pillasch et al. (1997) used fluorescence in situ hybridization to map the MSS4 gene to human chromosome 1q32-q41.

[55307] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55308] Muller-Pillasch, F.; Zimmerhackl, F.; Lacher, U.; Schultz, N.; Hameister, H.; Varga, G.; Friess, H.; Buchler, M.; Adler, G.; Gress, T. M. : Cloning of novel transcripts of the hu-

man guanine–nucleotide–exchange factor Mss4: in situ chromosomal mapping and expression in pancreatic cancer. Genomics 46: 389–396, 1997. ; and

[55309] Yu, H.; Schreiber, S. L. : Cloning, Zn(2+) binding, and structural characterization of the guanine nucleotide exchange factor human Mss4. Biochemistry 34: 9103–9110, 1995.

[55310] Further studies establishing the function and utilities of RABIF are found in John Hopkins OMIM database record ID 603417, and in cited publications numbered 8184–8185 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0596 (Accession XM\_031706) is another VGAM1633 host target gene. KIAA0596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0596 BINDING SITE, designated SEQ ID:31461, to the nucleotide sequence of VGAM1633 RNA, herein designated VGAM RNA, also designated SEQ ID:4344.

[55311] Another function of VGAM1633 is therefore inhibition of

KIAA0596 (Accession XM\_031706). Accordingly, utilities of VGAM1633 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0596. LOC144501 (Accession XM\_096612) is another VGAM1633 host target gene. LOC144501 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144501 BINDING SITE, designated SEQ ID:40425, to the nucleotide sequence of VGAM1633 RNA, herein designated VGAM RNA, also designated SEQ ID:4344.

[55312] Another function of VGAM1633 is therefore inhibition of LOC144501 (Accession XM\_096612). Accordingly, utilities of VGAM1633 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144501. LOC163412 (Accession XM\_088868) is another VGAM1633 host target gene. LOC163412 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163412, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC163412 BINDING SITE, designated SEQ ID:39955, to the nucleotide sequence of VGAM1633 RNA, herein designated VGAM RNA, also designated SEQ ID:4344.

[55313] Another function of VGAM1633 is therefore inhibition of LOC163412 (Accession XM\_088868). Accordingly, utilities of VGAM1633 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163412. LOC222182 (Accession XM\_168471) is another VGAM1633 host target gene. LOC222182 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222182 BINDING SITE, designated SEQ ID:45197, to the nucleotide sequence of VGAM1633 RNA, herein designated VGAM RNA, also designated SEQ ID:4344.

[55314] Another function of VGAM1633 is therefore inhibition of LOC222182 (Accession XM\_168471). Accordingly, utilities of VGAM1633 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222182. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1634 (VGAM1634) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55315] VGAM1634 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1634 was detected is described hereinabove with reference to Figs. 1–8.

[55316] VGAM1634 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1634 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55317] VGAM1634 gene encodes a VGAM1634 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1634 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1634 precursor RNA is designated SEQ ID:1620, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1620 is located at position 81295 relative to the genome of Bovine Herpesvirus 4.

[55318] VGAM1634 precursor RNA folds onto itself, forming VGAM1634 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55319] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1634 folded precursor RNA into VGAM1634 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1634 RNA is designated SEQ ID:4345, and is provided hereinbelow with reference to the sequence listing part.

[55320] VGAM1634 host target gene, herein designated VGAM



HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1634 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1634 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55321] VGAM1634 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1634 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1634 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1634 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1634 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[55322] The complementary binding of VGAM1634 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1634 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1634 host target RNA into VGAM1634 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55323] It is appreciated that VGAM1634 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1634 host target genes. The mRNA of each one of this plurality of VGAM1634 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1634 RNA, herein designated VGAM RNA, and which when bound by VGAM1634 RNA causes inhibition of translation of respective one or more

VGAM1634 host target proteins.

[55324] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1634 gene, herein designated VGAM GENE, on one or more VGAM1634 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55325] It is yet further appreciated that a function of VGAM1634 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Spe-

cific functions, and accordingly utilities, of VGAM1634 correlate with, and may be deduced from, the identity of the host target genes which VGAM1634 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55326] Nucleotide sequences of the VGAM1634 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1634 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1634 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1634 are further described hereinbelow with reference to Table 1.

[55327] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1634 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1634 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55328] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1634 gene, herein designated VGAM is inhibition of expression of VGAM1634 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1634 correlate with, and may be deduced from, the identity of the target genes which VGAM1634 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55329] Nuclear Receptor Subfamily 5, Group A, Member 2 (NR5A2, Accession NM\_003822) is a VGAM1634 host target gene. NR5A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NR5A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR5A2 BINDING SITE, designated SEQ ID:9915, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55330] A function of VGAM1634 is therefore inhibition of Nuclear Receptor Subfamily 5, Group A, Member 2 (NR5A2, Accession NM\_003822), a gene which is a member of nuclear receptor superfamily of transcriptional activators and activates the hepatitis B virus (HBV) promoter. Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR5A2. The function of NR5A2 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM375. Wingless-type MMTV Integration Site Family, Member 3A (WNT3A, Accession NM\_033131) is another VGAM1634 host target gene. WNT3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WNT3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT3A BINDING SITE, designated SEQ ID:26973, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55331] Another function of VGAM1634 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 3A (WNT3A, Accession NM\_033131). Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT3A. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM\_033332) is another VGAM1634 host target gene. CDC14B BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by CDC14B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE, designated SEQ ID:27166, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55332] Another function of VGAM1634 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM\_033332). Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. KIAA1656 (Accession XM\_038022) is another VGAM1634 host target gene. KIAA1656 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1656 BINDING SITE, designated SEQ ID:32727, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55333] Another function of VGAM1634 is therefore inhibition of

KIAA1656 (Accession XM\_038022). Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1656. PRO1914 (Accession NM\_014106) is another VGAM1634 host target gene. PRO1914 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1914, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1914 BINDING SITE, designated SEQ ID:15329, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55334] Another function of VGAM1634 is therefore inhibition of PRO1914 (Accession NM\_014106). Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1914. PRO2859 (Accession NM\_018543) is another VGAM1634 host target gene. PRO2859 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO2859, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-



plementarity of the nucleotide sequences of PRO2859 BINDING SITE, designated SEQ ID:20616, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55335] Another function of VGAM1634 is therefore inhibition of PRO2859 (Accession NM\_018543). Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2859. RDH-E2 (Accession NM\_138969) is another VGAM1634 host target gene. RDH-E2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RDH-E2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDH-E2 BINDING SITE, designated SEQ ID:29079, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55336] Another function of VGAM1634 is therefore inhibition of RDH-E2 (Accession NM\_138969). Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDH-E2. LOC131583 (Accession XM\_067456) is another

VGAM1634 host target gene. LOC131583 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC131583, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131583 BINDING SITE, designated SEQ ID:37356, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55337] Another function of VGAM1634 is therefore inhibition of LOC131583 (Accession XM\_067456). Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131583. LOC204593 (Accession XM\_119002) is another VGAM1634 host target gene. LOC204593 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204593, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204593 BINDING SITE, designated SEQ ID:43583, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55338] Another function of VGAM1634 is therefore inhibition of LOC204593 (Accession XM\_119002). Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204593. LOC254042 (Accession XM\_171022) is another VGAM1634 host target gene. LOC254042 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254042 BINDING SITE, designated SEQ ID:45791, to the nucleotide sequence of VGAM1634 RNA, herein designated VGAM RNA, also designated SEQ ID:4345.

[55339] Another function of VGAM1634 is therefore inhibition of LOC254042 (Accession XM\_171022). Accordingly, utilities of VGAM1634 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254042. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1635 (VGAM1635) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[55340] VGAM1635 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1635 was detected is described hereinabove with reference to Figs. 1–8.

[55341] VGAM1635 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1635 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55342] VGAM1635 gene encodes a VGAM1635 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1635 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1635 precursor RNA is designated SEQ ID:1621, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1621 is located at position 121659 relative to the genome of Human Herpesvirus 8.

[55343] VGAM1635 precursor RNA folds onto itself, forming VGAM1635 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55344] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1635 folded precursor RNA into VGAM1635 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1635 RNA is designated SEQ ID:4346, and is provided hereinbelow with reference to the sequence listing part.

[55345] VGAM1635 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1635 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1635 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55346] VGAM1635 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1635 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1635 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1635 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1635 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55347] The complementary binding of VGAM1635 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1635 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1635 host target RNA into VGAM1635 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55348] It is appreciated that VGAM1635 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1635 host target genes. The mRNA of each one of this plurality of VGAM1635 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1635 RNA, herein designated VGAM RNA, and which when bound by VGAM1635 RNA causes inhibition of translation of respective one or more VGAM1635 host target proteins.

[55349] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1635 gene, herein designated VGAM GENE, on one or more VGAM1635 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55350] It is yet further appreciated that a function of VGAM1635 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1635 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1635 correlate with, and may be deduced from, the identity of the host target genes which VGAM1635 binds and inhibits, and the function of these host target genes, as



elaborated hereinbelow.

[55351] Nucleotide sequences of the VGAM1635 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1635 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1635 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1635 are further described hereinbelow with reference to Table 1.

[55352] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1635 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1635 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55353] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1635 gene, herein designated VGAM is inhibition of expression of VGAM1635 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1635 correlate with, and may be deduced from, the identity of the target genes which VGAM1635 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55354] Crn, Crooked Neck-like 1 (Drosophila) (CRNKL1, Accession NM\_016652) is a VGAM1635 host target gene. CRNKL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRNKL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRNKL1 BINDING SITE, designated SEQ ID:18771, to the nucleotide sequence of VGAM1635 RNA, herein designated VGAM RNA, also designated SEQ ID:4346.

[55355] A function of VGAM1635 is therefore inhibition of Crn, Crooked Neck-like 1 (Drosophila) (CRNKL1, Accession NM\_016652). Accordingly, utilities of VGAM1635 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRNKL1. KIAA1190 (Accession XM\_048695) is another VGAM1635 host target gene. KIAA1190 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1190 BINDING SITE, designated

SEQ ID:35223, to the nucleotide sequence of VGAM1635 RNA, herein designated VGAM RNA, also designated SEQ ID:4346.

[55356] Another function of VGAM1635 is therefore inhibition of KIAA1190 (Accession XM\_048695). Accordingly, utilities of VGAM1635 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1190. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1636 (VGAM1636) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55357] VGAM1636 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1636 was detected is described hereinabove with reference to Figs. 1–8.

[55358] VGAM1636 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1636 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55359] VGAM1636 gene encodes a VGAM1636 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1636 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1636 precursor RNA is designated SEQ ID:1622, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1622 is located at position 119152 relative to the genome of Human Herpesvirus 8.

[55360] VGAM1636 precursor RNA folds onto itself, forming VGAM1636 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55361] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1636 folded precursor RNA into VGAM1636 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1636 RNA is designated SEQ ID:4347, and is provided hereinbelow with reference to the sequence listing part.

[55362] VGAM1636 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1636 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1636 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55363] VGAM1636 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1636 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1636 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1636 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1636 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55364] The complementary binding of VGAM1636 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1636 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1636 host target RNA into VGAM1636 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55365] It is appreciated that VGAM1636 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1636 host target genes. The mRNA of each one of this plurality of VGAM1636 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1636 RNA, herein designated VGAM RNA, and which when bound by VGAM1636 RNA causes inhibition of translation of respective one or more VGAM1636 host target proteins.

[55366] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1636 gene, herein designated VGAM GENE, on one or more VGAM1636 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[55367] It is yet further appreciated that a function of VGAM1636 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1636 correlate with, and may be deduced from, the identity of the host target genes which VGAM1636 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55368] Nucleotide sequences of the VGAM1636 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1636 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1636 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1636 are further described hereinbelow with reference to Table 1.

[55369] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1636 host target RNA, and



schematic representation of the complementarity of each of these host target binding sites to VGAM1636 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55370] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1636 gene, herein designated VGAM is inhibition of expression of VGAM1636 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1636 correlate with, and may be deduced from, the identity of the target genes which VGAM1636 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55371] Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM\_005093) is a VGAM1636 host target gene. CBFA2T2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFA2T2 BINDING SITE, designated SEQ ID:11545, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55372] A function of VGAM1636 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM\_005093), a gene which is a putative transcription factor. Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T2. The function of CBFA2T2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. DNA Fragmentation Factor, 40kDa, Beta Polypeptide (caspase-activated DNase) (DFFB, Accession XM\_113366) is another VGAM1636 host target gene. DFFB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DFFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DFFB BINDING SITE, designated SEQ ID:42236, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55373] Another function of VGAM1636 is therefore inhibition of DNA Fragmentation Factor, 40kDa, Beta Polypeptide

(caspase-activated DNase) (DFFB, Accession XM\_113366), a gene which induces DNA fragmentation and chromatin condensation during apoptosis. Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DFFB. The function of DFFB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Deleted In Lung and Esophageal Cancer 1 (DLEC1, Accession NM\_007336) is another VGAM1636 host target gene. DLEC1 BINDING SITE1 and DLEC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DLEC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLEC1 BINDING SITE1 and DLEC1 BINDING SITE2, designated SEQ ID:14261 and SEQ ID:14267 respectively, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55374] Another function of VGAM1636 is therefore inhibition of Deleted In Lung and Esophageal Cancer 1 (DLEC1, Accession NM\_007336). Accordingly, utilities of VGAM1636 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with DLEC1. Mediterranean Fever (MEFV, Accession NM\_000243) is another VGAM1636 host target gene. MEFV BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MEFV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEFV BINDING SITE, designated SEQ ID:5766, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55375] Another function of VGAM1636 is therefore inhibition of Mediterranean Fever (MEFV, Accession NM\_000243). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEFV. MHC Class I Polypeptide-related Sequence B (MICB, Accession NM\_005931) is another VGAM1636 host target gene. MICB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MICB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MICB BINDING SITE, designated SEQ ID:5767, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

tarity of the nucleotide sequences of MICB BINDING SITE, designated SEQ ID:12563, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55376] Another function of VGAM1636 is therefore inhibition of MHC Class I Polypeptide-related Sequence B (MICB, Accession NM\_005931), a gene which involved in the presentation of foreign antigens to the immune system. Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MICB. The function of MICB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Melan-A (MLANA, Accession NM\_005511) is another VGAM1636 host target gene. MLANA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLANA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLANA BINDING SITE, designated SEQ ID:12026, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ

ID:4347.

[55377] Another function of VGAM1636 is therefore inhibition of Melan-A (MLANA, Accession NM\_005511). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLANA. NDRG Family Member 3 (NDRG3, Accession NM\_032013) is another VGAM1636 host target gene. NDRG3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDRG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG3 BINDING SITE, designated SEQ ID:25719, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55378] Another function of VGAM1636 is therefore inhibition of NDRG Family Member 3 (NDRG3, Accession NM\_032013). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG3. NAD(P)H Dehydrogenase, Quinone 1 (NQO1, Accession NM\_000903) is another VGAM1636 host target gene. NQO1 BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by NQO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NQO1 BINDING SITE, designated SEQ ID:6604, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55379] Another function of VGAM1636 is therefore inhibition of NAD(P)H Dehydrogenase, Quinone 1 (NQO1, Accession NM\_000903), a gene which is cytochrome b5 reductase which reduces redox dyes and quinones. Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NQO1. The function of NQO1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM923. Pre-B-cell Leukemia Transcription Factor 2 (PBX2, Accession NM\_002586) is another VGAM1636 host target gene. PBX2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PBX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PBX2 BINDING SITE, designated SEQ ID:8449, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55380] Another function of VGAM1636 is therefore inhibition of Pre-B-cell Leukemia Transcription Factor 2 (PBX2, Accession NM\_002586), a gene which binds the sequence 5'-atcaatcaa-3'. Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PBX2. The function of PBX2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1063. Period Homolog 2 (Drosophila) (PER2, Accession NM\_022817) is another VGAM1636 host target gene. PER2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER2 BINDING SITE, designated SEQ ID:23089, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA,



also designated SEQ ID:4347.

[55381] Another function of VGAM1636 is therefore inhibition of Period Homolog 2 (Drosophila) (PER2, Accession NM\_022817), a gene which Period homolog 2; putative circadian clock protein; has a PAS dimerization domain. Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER2. The function of PER2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Palmitoyl-protein Thioesterase 1 (ceroid-lipofuscinosis, neuronal 1, infantile) (PPT1, Accession XM\_029842) is another VGAM1636 host target gene. PPT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPT1 BINDING SITE, designated SEQ ID:30954, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55382] Another function of VGAM1636 is therefore inhibition of

Palmitoyl-protein Thioesterase 1 (ceroid-lipofuscinosis, neuronal 1, infantile) (PPT1, Accession XM\_029842). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPT1. Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 9 (PSMD9, Accession NM\_002813) is another VGAM1636 host target gene. PSMD9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMD9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMD9 BINDING SITE, designated SEQ ID:8677, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55383] Another function of VGAM1636 is therefore inhibition of Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 9 (PSMD9, Accession NM\_002813), a gene which acts as a regulatory subunit of the 26 proteasome. Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMD9. The function of PSMD9 has been

established by previous studies. The 26S proteasome is a eukaryotic ATP-dependent protease that selectively degrades intracellular target proteins that are modified by the covalent attachment of ubiquitin. It is composed of a central catalytic 20S proteasome, which consists of a family of small proteins, and 2 large regulatory modules, named PA700, which consist of approximately 20 heterogeneous proteins. A proteasomal modulator complex, composed of p27, p42, and p50 subunits, stimulates the association of the 20S proteasome with PA700 to form the active 26S proteasome. Watanabe et al. (1998) cloned 2 distinct human brain cDNAs encoding p27, or PSMD9. Compared with the longer cDNA, the shorter cDNA has a 65-bp deletion near the 3-prime region that results in a new inframe termination codon farther downstream. The longer cDNA encodes a deduced 209-amino acid protein with a calculated molecular mass of 22,764 Da. The shorter cDNA encodes a deduced 223-amino acid protein with a calculated molecular mass of 24,652 Da. The longer PSMD9 protein exhibits 36% sequence identity with an *S. cerevisiae* protein, which the authors named NAS2 for 'non-ATPase subunit 2,' and 31.9% identity with a *C. elegans* protein. Disruption of the yeast NAS2 gene did

not affect cell viability or proliferation. Watanabe et al. (1998) demonstrated that the PSMD9 protein, along with the ATPase components TBP1 (PSMC3; 186852) and p42 (PSMC6; 602708), associated with both the modulator complex and the 26S proteasome complex. Northern blot analysis detected an approximately 1.3-kb PSMD9 transcript in all tissues examined, with highest levels in liver and kidney. E12 and E47 (see OMIM Ref. No. TCF3; 147141), members of the ubiquitous E2A protein family, function with basic helix-loop-helix (bHLH) proteins to bind and transactivate promoters via conserved sequence elements known as E boxes. By yeast 2-hybrid screening of a rat insulinoma cell cDNA library using the bHLH domain-containing C terminus of E12 as bait, Thomas et al. (1999) obtained a cDNA encoding rat Bridge-1. Sequence analysis predicted that the 222-amino acid Bridge-1 protein shares 98% amino acid similarity with human PSMD9 over the first 184 amino acids but diverges in the C terminus. Bridge-1 contains a PDZ-like domain from amino acids 138 to 178, forming 3 beta sheets and 2 alpha helices. SDS-PAGE analysis showed that Bridge-1 is expressed as a 28-kD protein, close to the deduced value of 25 kD. Using Bridge-1 cDNA as probe, Northern blot anal-

ysis detected a 1.0-kb transcript in all rat and human tissues tested, with highest expression in pancreas, testis, kidney, and liver. Immunocytochemistry assessment demonstrated predominant nuclear localization of Bridge-1, with lower levels in cytoplasm. Immunoprecipitation analysis determined that anti-Bridge-1 coimmunoprecipitates E12 or E12 and E47 through their C-terminal bHLH domains, but only in the presence of the PDZ domain of Bridge-1. CAT assays indicated that Bridge-1 together with E12 or E47 coactivates insulin (OMIM Ref. No. 176730) promoter elements.

[55384] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55385] Thomas, M. K.; Yao, K.-M.; Tenser, M. S.; Wong, G. G.; Habener, J. F. : Bridge-1, a novel PDZ-domain coactivator of E2A-mediated regulation of insulin gene transcription. *Molec. Cell. Biol.* 19: 8492-8504, 1999. ; and

[55386] Watanabe, T. K.; Saito, A.; Suzuki, M.; Fujiwara, T.; Takahashi, E.; Slaughter, C. A.; DeMartino, G. N.; Hendil, K. B.; Chung, C. H.; Tanahashi, N.; Tanaka, K. : cDNA cloning and chara.

[55387] Further studies establishing the function and utilities of

PSMD9 are found in John Hopkins OMIM database record ID 603146, and in cited publications numbered 5426–5427 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sex Comb On Midleg-like 2 (Drosophila) (SCML2, Accession NM\_006089) is another VGAM1636 host target gene. SCML2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SCML2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCML2 BINDING SITE, designated SEQ ID:12733, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55388] Another function of VGAM1636 is therefore inhibition of Sex Comb On Midleg-like 2 (Drosophila) (SCML2, Accession NM\_006089). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCML2. Selenoprotein X, 1 (SEPX1, Accession NM\_016332) is another VGAM1636 host target gene. SEPX1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by SEPX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPX1 BINDING SITE, designated SEQ ID:18456, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55389] Another function of VGAM1636 is therefore inhibition of Selenoprotein X, 1 (SEPX1, Accession NM\_016332). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPX1. Sulfotransferase Family, Cytosolic, 2B, Member 1 (SULT2B1, Accession NM\_004605) is another VGAM1636 host target gene. SULT2B1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SULT2B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SULT2B1 BINDING SITE, designated SEQ ID:10948, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55390] Another function of VGAM1636 is therefore inhibition of

Sulfotransferase Family, Cytosolic, 2B, Member 1 (SULT2B1, Accession NM\_004605). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SULT2B1. Von Hippel–Lindau Syndrome (VHL, Accession NM\_000551) is another VGAM1636 host target gene. VHL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VHL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VHL BINDING SITE, designated SEQ ID:6154, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55391] Another function of VGAM1636 is therefore inhibition of Von Hippel–Lindau Syndrome (VHL, Accession NM\_000551), a gene which may control rna stability through the selective degradation of rna-bound proteins. Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VHL. The function of VHL and its association with various diseases and clinical conditions, has been established by previous studies, as described here–



in above with reference to VGAM197. Activating Transcription Factor 3 (ATF3, Accession NM\_004024) is another VGAM1636 host target gene. ATF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATF3 BINDING SITE, designated SEQ ID:10246, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55392] Another function of VGAM1636 is therefore inhibition of Activating Transcription Factor 3 (ATF3, Accession NM\_004024). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATF3. BOP (Accession XM\_097915) is another VGAM1636 host target gene. BOP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BOP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BOP BINDING SITE, designated SEQ ID:41209, to the nu-

cleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55393] Another function of VGAM1636 is therefore inhibition of BOP (Accession XM\_097915). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BOP. CED-6 (Accession NM\_016315) is another VGAM1636 host target gene. CED-6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CED-6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CED-6 BINDING SITE, designated SEQ ID:18429, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55394] Another function of VGAM1636 is therefore inhibition of CED-6 (Accession NM\_016315). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CED-6. CXYorf1 (Accession XM\_088704) is another VGAM1636 host target gene. CXYorf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by CXYorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXYorf1 BINDING SITE, designated SEQ ID:39912, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55395] Another function of VGAM1636 is therefore inhibition of CXYorf1 (Accession XM\_088704). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXYorf1. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681) is another VGAM1636 host target gene. DDX34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE, designated SEQ ID:16168, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55396] Another function of VGAM1636 is therefore inhibition of

DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. Ecotropic Viral Integration Site 5 (EVI5, Accession NM\_005665) is another VGAM1636 host target gene. EVI5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EVI5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVI5 BINDING SITE, designated SEQ ID:12205, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55397] Another function of VGAM1636 is therefore inhibition of Ecotropic Viral Integration Site 5 (EVI5, Accession NM\_005665). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVI5. FBP17 (Accession XM\_052666) is another VGAM1636 host target gene. FBP17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBP17, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBP17 BINDING SITE, designated SEQ ID:36045, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55398] Another function of VGAM1636 is therefore inhibition of FBP17 (Accession XM\_052666). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBP17. FLJ10159 (Accession NM\_018013) is another VGAM1636 host target gene. FLJ10159 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10159 BINDING SITE, designated SEQ ID:19747, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55399] Another function of VGAM1636 is therefore inhibition of FLJ10159 (Accession NM\_018013). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ10159. FLJ12363 (Accession NM\_032167) is another VGAM1636 host target gene. FLJ12363 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12363, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12363 BINDING SITE, designated SEQ ID:25864, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55400] Another function of VGAM1636 is therefore inhibition of FLJ12363 (Accession NM\_032167). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12363. FLJ12816 (Accession NM\_022060) is another VGAM1636 host target gene. FLJ12816 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12816, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12816 BINDING SITE, designated SEQ ID:22605, to the nucleotide

sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55401] Another function of VGAM1636 is therefore inhibition of FLJ12816 (Accession NM\_022060). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12816. FLJ12891 (Accession NM\_024950) is another VGAM1636 host target gene. FLJ12891 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12891 BINDING SITE, designated SEQ ID:24508, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55402] Another function of VGAM1636 is therefore inhibition of FLJ12891 (Accession NM\_024950). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12891. FLJ20241 (Accession NM\_017721) is another VGAM1636 host target gene. FLJ20241 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by FLJ20241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20241 BINDING SITE, designated SEQ ID:19311, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55403] Another function of VGAM1636 is therefore inhibition of FLJ20241 (Accession NM\_017721). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20241. FLJ21168 (Accession NM\_025073) is another VGAM1636 host target gene. FLJ21168 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21168, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21168 BINDING SITE, designated SEQ ID:24670, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55404] Another function of VGAM1636 is therefore inhibition of FLJ21168 (Accession NM\_025073). Accordingly, utilities of



VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21168. FLJ22684 (Accession NM\_025048) is another VGAM1636 host target gene. FLJ22684 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22684, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22684 BINDING SITE, designated SEQ ID:24642, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55405] Another function of VGAM1636 is therefore inhibition of FLJ22684 (Accession NM\_025048). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22684. KIAA0161 (Accession NM\_014746) is another VGAM1636 host target gene. KIAA0161 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0161 BINDING SITE, designated SEQ ID:16427, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55406] Another function of VGAM1636 is therefore inhibition of KIAA0161 (Accession NM\_014746). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0161. KIAA0391 (Accession NM\_014672) is another VGAM1636 host target gene. KIAA0391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0391 BINDING SITE, designated SEQ ID:16133, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55407] Another function of VGAM1636 is therefore inhibition of KIAA0391 (Accession NM\_014672). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0391. KIAA0472 (Accession XM\_050147) is another VGAM1636 host target gene. KIAA0472 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0472, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0472 BINDING SITE, designated SEQ ID:35581, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55408] Another function of VGAM1636 is therefore inhibition of KIAA0472 (Accession XM\_050147). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0472. KIAA1170 (Accession XM\_045907) is another VGAM1636 host target gene. KIAA1170 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1170 BINDING SITE, designated SEQ ID:34609, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55409] Another function of VGAM1636 is therefore inhibition of

KIAA1170 (Accession XM\_045907). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1170. KIAA1198 (Accession XM\_032674) is another VGAM1636 host target gene. KIAA1198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1198 BINDING SITE, designated SEQ ID:31699, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55410] Another function of VGAM1636 is therefore inhibition of KIAA1198 (Accession XM\_032674). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. KIAA1493 (Accession XM\_034415) is another VGAM1636 host target gene. KIAA1493 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1493 BINDING SITE, designated SEQ ID:32085, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55411] Another function of VGAM1636 is therefore inhibition of KIAA1493 (Accession XM\_034415). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1493. KIAA1712 (Accession XM\_041497) is another VGAM1636 host target gene. KIAA1712 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1712, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1712 BINDING SITE, designated SEQ ID:33535, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55412] Another function of VGAM1636 is therefore inhibition of KIAA1712 (Accession XM\_041497). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1712. MGC35558 (Accession NM\_145013) is another

VGAM1636 host target gene. MGC35558 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC35558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC35558 BINDING SITE, designated SEQ ID:29615, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55413] Another function of VGAM1636 is therefore inhibition of MGC35558 (Accession NM\_145013). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC35558. MGC4730 (Accession XM\_034644) is another VGAM1636 host target gene. MGC4730 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4730, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4730 BINDING SITE, designated SEQ ID:32134, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55414] Another function of VGAM1636 is therefore inhibition of MGC4730 (Accession XM\_034644). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4730. PIP3-E (Accession XM\_039749) is another VGAM1636 host target gene. PIP3-E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP3-E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP3-E BINDING SITE, designated SEQ ID:33173, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55415] Another function of VGAM1636 is therefore inhibition of PIP3-E (Accession XM\_039749). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP3-E. PRO2955 (Accession NM\_018545) is another VGAM1636 host target gene. PRO2955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2955 BINDING SITE, designated SEQ ID:20619, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55416] Another function of VGAM1636 is therefore inhibition of PRO2955 (Accession NM\_018545). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2955. Proline-serine-threonine Phosphatase Interacting Protein 2 (PSTPIP2, Accession NM\_024430) is another VGAM1636 host target gene. PSTPIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSTPIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSTPIP2 BINDING SITE, designated SEQ ID:23678, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55417] Another function of VGAM1636 is therefore inhibition of Proline-serine-threonine Phosphatase Interacting Protein 2 (PSTPIP2, Accession NM\_024430). Accordingly, utilities



of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSTPIP2. Ubiquitin-conjugating Enzyme E2 Variant 2 (UBE2V2, Accession NM\_003350) is another VGAM1636 host target gene. UBE2V2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2V2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2V2 BINDING SITE, designated SEQ ID:9376, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55418] Another function of VGAM1636 is therefore inhibition of Ubiquitin-conjugating Enzyme E2 Variant 2 (UBE2V2, Accession NM\_003350). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2V2. VDU1 (Accession NM\_015017) is another VGAM1636 host target gene. VDU1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VDU1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of VDU1 BINDING SITE, designated SEQ ID:17380, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55419] Another function of VGAM1636 is therefore inhibition of VDU1 (Accession NM\_015017). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VDU1. Vacuolar Protein Sorting 33A (yeast) (VPS33A, Accession NM\_022916) is another VGAM1636 host target gene. VPS33A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VPS33A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VPS33A BINDING SITE, designated SEQ ID:23229, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55420] Another function of VGAM1636 is therefore inhibition of Vacuolar Protein Sorting 33A (yeast) (VPS33A, Accession NM\_022916). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with VPS33A. Williams–Beuren Syndrome Chromosome Region 23 (WBSCR23, Accession NM\_025042) is another VGAM1636 host target gene. WBSCR23 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by WBSCR23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WBSCR23 BINDING SITE, designated SEQ ID:24636, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55421] Another function of VGAM1636 is therefore inhibition of Williams–Beuren Syndrome Chromosome Region 23 (WBSCR23, Accession NM\_025042). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WBSCR23. LOC133362 (Accession XM\_068305) is another VGAM1636 host target gene. LOC133362 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC133362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC133362 BINDING SITE, designated SEQ ID:37380, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55422] Another function of VGAM1636 is therefore inhibition of LOC133362 (Accession XM\_068305). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133362. LOC143916 (Accession XM\_084664) is another VGAM1636 host target gene. LOC143916 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143916 BINDING SITE, designated SEQ ID:37649, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55423] Another function of VGAM1636 is therefore inhibition of LOC143916 (Accession XM\_084664). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143916. LOC144524 (Accession XM\_096624) is an-

other VGAM1636 host target gene. LOC144524 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144524, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144524 BINDING SITE, designated SEQ ID:40432, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55424] Another function of VGAM1636 is therefore inhibition of LOC144524 (Accession XM\_096624). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144524. LOC146229 (Accession XM\_085387) is another VGAM1636 host target gene. LOC146229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146229 BINDING SITE, designated SEQ ID:38103, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55425] Another function of VGAM1636 is therefore inhibition of LOC146229 (Accession XM\_085387). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146229. LOC149711 (Accession XM\_097720) is another VGAM1636 host target gene. LOC149711 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149711 BINDING SITE, designated SEQ ID:41066, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55426] Another function of VGAM1636 is therefore inhibition of LOC149711 (Accession XM\_097720). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149711. LOC169611 (Accession XM\_095809) is another VGAM1636 host target gene. LOC169611 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169611, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169611 BINDING SITE, designated SEQ ID:40284, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55427] Another function of VGAM1636 is therefore inhibition of LOC169611 (Accession XM\_095809). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169611. LOC196047 (Accession XM\_116883) is another VGAM1636 host target gene. LOC196047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196047 BINDING SITE, designated SEQ ID:43142, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55428] Another function of VGAM1636 is therefore inhibition of LOC196047 (Accession XM\_116883). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196047. LOC196510 (Accession XM\_113738) is another VGAM1636 host target gene. LOC196510 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196510, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196510 BINDING SITE, designated SEQ ID:42392, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55429] Another function of VGAM1636 is therefore inhibition of LOC196510 (Accession XM\_113738). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196510. LOC199699 (Accession XM\_113990) is another VGAM1636 host target gene. LOC199699 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199699, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199699 BINDING SITE, designated SEQ ID:42593, to the nucleotide sequence of VGAM1636 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4347.

[55430] Another function of VGAM1636 is therefore inhibition of LOC199699 (Accession XM\_113990). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199699. LOC199958 (Accession XM\_117163) is another VGAM1636 host target gene. LOC199958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199958 BINDING SITE, designated SEQ ID:43263, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55431] Another function of VGAM1636 is therefore inhibition of LOC199958 (Accession XM\_117163). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199958. LOC200093 (Accession XM\_032184) is another VGAM1636 host target gene. LOC200093 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200093, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200093 BINDING SITE, designated SEQ ID:31604, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55432] Another function of VGAM1636 is therefore inhibition of LOC200093 (Accession XM\_032184). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200093. LOC200220 (Accession XM\_114157) is another VGAM1636 host target gene. LOC200220 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200220 BINDING SITE, designated SEQ ID:42741, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55433] Another function of VGAM1636 is therefore inhibition of LOC200220 (Accession XM\_114157). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC200220. LOC220074 (Accession NM\_145309) is another VGAM1636 host target gene. LOC220074 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220074 BINDING SITE, designated SEQ ID:29821, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55434] Another function of VGAM1636 is therefore inhibition of LOC220074 (Accession NM\_145309). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220074. LOC222160 (Accession XM\_168431) is another VGAM1636 host target gene. LOC222160 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222160 BINDING SITE, designated SEQ ID:45163, to

the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55435] Another function of VGAM1636 is therefore inhibition of LOC222160 (Accession XM\_168431). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222160. LOC256364 (Accession XM\_170672) is another VGAM1636 host target gene. LOC256364 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256364, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256364 BINDING SITE, designated SEQ ID:45444, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55436] Another function of VGAM1636 is therefore inhibition of LOC256364 (Accession XM\_170672). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256364. LOC91040 (Accession XM\_035641) is another VGAM1636 host target gene. LOC91040 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC91040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91040 BINDING SITE, designated SEQ ID:32321, to the nucleotide sequence of VGAM1636 RNA, herein designated VGAM RNA, also designated SEQ ID:4347.

[55437] Another function of VGAM1636 is therefore inhibition of LOC91040 (Accession XM\_035641). Accordingly, utilities of VGAM1636 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91040. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1637 (VGAM1637) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55438] VGAM1637 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1637 was detected is described hereinabove with reference to Figs. 1-8.

[55439] VGAM1637 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human Herpesvirus 8. VGAM1637 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55440] VGAM1637 gene encodes a VGAM1637 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1637 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1637 precursor RNA is designated SEQ ID:1623, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1623 is located at position 122480 relative to the genome of Human Herpesvirus 8.

[55441] VGAM1637 precursor RNA folds onto itself, forming VGAM1637 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55442] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1637 folded precursor RNA into VGAM1637 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 63%) nucleotide sequence of VGAM1637 RNA is designated SEQ ID:4348, and is provided hereinbelow with reference to the sequence listing part.

[55443] VGAM1637 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1637 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1637 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55444] VGAM1637 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1637 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1637 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1637 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1637 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55445] The complementary binding of VGAM1637 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1637 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1637



host target RNA into VGAM1637 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55446] It is appreciated that VGAM1637 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1637 host target genes. The mRNA of each one of this plurality of VGAM1637 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1637 RNA, herein designated VGAM RNA, and which when bound by VGAM1637 RNA causes inhibition of translation of respective one or more VGAM1637 host target proteins.

[55447] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1637 gene, herein designated VGAM GENE, on one or more VGAM1637 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55448] It is yet further appreciated that a function of VGAM1637 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1637 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1637 correlate with, and may be deduced from, the identity of the host target genes which VGAM1637 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55449] Nucleotide sequences of the VGAM1637 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1637 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1637 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1637 are further

described hereinbelow with reference to Table 1.

[55450] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1637 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1637 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55451] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1637 gene, herein designated VGAM is inhibition of expression of VGAM1637 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1637 correlate with, and may be deduced from, the identity of the target genes which VGAM1637 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55452] Golgi Reassembly Stacking Protein 1, 65kDa (GORASP1, Accession NM\_031899) is a VGAM1637 host target gene. GORASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GORASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of GORASP1 BINDING SITE, designated SEQ ID:25643, to the nucleotide sequence of VGAM1637 RNA, herein designated VGAM RNA, also designated SEQ ID:4348.

[55453] A function of VGAM1637 is therefore inhibition of Golgi Reassembly Stacking Protein 1, 65kDa (GORASP1, Accession NM\_031899), a gene which has some function with the Golgi apparatus. Accordingly, utilities of VGAM1637 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GORASP1. The function of GORASP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM630.KIAA0884 (Accession XM\_046660) is another VGAM1637 host target gene. KIAA0884 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0884, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0884 BINDING SITE, designated SEQ ID:34771, to the nucleotide sequence of VGAM1637 RNA, herein designated VGAM RNA, also designated SEQ ID:4348.

[55454] Another function of VGAM1637 is therefore inhibition of KIAA0884 (Accession XM\_046660). Accordingly, utilities of VGAM1637 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0884. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1638 (VGAM1638) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55455] VGAM1638 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1638 was detected is described hereinabove with reference to Figs. 1–8.

[55456] VGAM1638 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1638 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55457] VGAM1638 gene encodes a VGAM1638 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1638 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1638 precursor RNA is designated SEQ ID:1624, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1624 is located at position 124374 relative to the genome of Human Herpesvirus 8.

[55458] VGAM1638 precursor RNA folds onto itself, forming VGAM1638 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55459] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1638 folded precursor RNA into VGAM1638 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1638 RNA is designated SEQ ID:4349, and is provided hereinbelow with reference to the sequence listing part.

[55460] VGAM1638 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1638 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1638 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[55461] VGAM1638 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1638 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1638 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1638 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1638 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55462] The complementary binding of VGAM1638 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1638 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1638 host target RNA into VGAM1638 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55463] It is appreciated that VGAM1638 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1638 host target genes. The mRNA of each one of this plurality of VGAM1638 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1638 RNA, herein designated VGAM RNA, and which when bound by VGAM1638 RNA causes inhibition of translation of respective one or more VGAM1638 host target proteins.

[55464] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1638 gene, herein designated VGAM GENE, on one or more VGAM1638 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55465] It is yet further appreciated that a function of VGAM1638 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1638 correlate with, and may be deduced from, the identity of the host target genes which VGAM1638 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55466] Nucleotide sequences of the VGAM1638 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1638 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1638 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1638 are further described hereinbelow with reference to Table 1.

[55467] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1638 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1638 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[55468] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1638 gene, herein designated VGAM is inhibition of expression of VGAM1638 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1638 correlate with, and may be deduced from, the identity of the target genes which VGAM1638 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55469] MLL Septin-like Fusion (MSF, Accession XM\_113892) is a VGAM1638 host target gene. MSF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSF BINDING SITE, designated SEQ ID:42519, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55470] A function of VGAM1638 is therefore inhibition of MLL Septin-like Fusion (MSF, Accession XM\_113892), a gene which plays a role in the cell cycle. Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MSF. The function of MSF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM514. Phosphorylase, Glycogen; Brain (PYGB, Accession NM\_002862) is another VGAM1638 host target gene. PYGB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PYGB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYGB BINDING SITE, designated SEQ ID:8763, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55471] Another function of VGAM1638 is therefore inhibition of Phosphorylase, Glycogen; Brain (PYGB, Accession NM\_002862). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYGB. Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM\_080821) is another VGAM1638 host target gene. C20orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

C20orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf108 BINDING SITE, designated SEQ ID:28086, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55472] Another function of VGAM1638 is therefore inhibition of Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM\_080821). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf108. FLJ10378 (Accession NM\_018078) is another VGAM1638 host target gene. FLJ10378 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10378, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10378 BINDING SITE, designated SEQ ID:19839, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55473] Another function of VGAM1638 is therefore inhibition of

FLJ10378 (Accession NM\_018078). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10378. HDCMA18P (Accession NM\_016648) is another VGAM1638 host target gene. HDCMA18P BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HDCMA18P, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDCMA18P BINDING SITE, designated SEQ ID:18766, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55474] Another function of VGAM1638 is therefore inhibition of HDCMA18P (Accession NM\_016648). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDCMA18P. KIAA0164 (Accession NM\_014739) is another VGAM1638 host target gene. KIAA0164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0164 BINDING SITE, designated SEQ ID:16403, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55475] Another function of VGAM1638 is therefore inhibition of KIAA0164 (Accession NM\_014739). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0164. SNF1 Sucrose Nonfermenting Like Kinase (yeast) (SLK, Accession NM\_014720) is another VGAM1638 host target gene. SLK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLK BINDING SITE, designated SEQ ID:16282, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55476] Another function of VGAM1638 is therefore inhibition of SNF1 Sucrose Nonfermenting Like Kinase (yeast) (SLK, Accession NM\_014720). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with SLK. LOC144811 (Accession XM\_096681) is another VGAM1638 host target gene. LOC144811 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144811 BINDING SITE, designated SEQ ID:40454, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55477] Another function of VGAM1638 is therefore inhibition of LOC144811 (Accession XM\_096681). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144811. LOC145786 (Accession XM\_096860) is another VGAM1638 host target gene. LOC145786 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145786 BINDING SITE, designated SEQ ID:40592, to



the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55478] Another function of VGAM1638 is therefore inhibition of LOC145786 (Accession XM\_096860). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145786. LOC158696 (Accession XM\_088644) is another VGAM1638 host target gene. LOC158696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158696 BINDING SITE, designated SEQ ID:39880, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55479] Another function of VGAM1638 is therefore inhibition of LOC158696 (Accession XM\_088644). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158696. LOC254556 (Accession XM\_170588) is another VGAM1638 host target gene. LOC254556 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC254556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254556 BINDING SITE, designated SEQ ID:45391, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55480] Another function of VGAM1638 is therefore inhibition of LOC254556 (Accession XM\_170588). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254556. LOC257415 (Accession XM\_171177) is another VGAM1638 host target gene. LOC257415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257415 BINDING SITE, designated SEQ ID:45958, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55481] Another function of VGAM1638 is therefore inhibition of LOC257415 (Accession XM\_171177). Accordingly, utilities

of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257415. LOC90342 (Accession XM\_031009) is another VGAM1638 host target gene. LOC90342 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90342 BINDING SITE, designated SEQ ID:31254, to the nucleotide sequence of VGAM1638 RNA, herein designated VGAM RNA, also designated SEQ ID:4349.

[55482] Another function of VGAM1638 is therefore inhibition of LOC90342 (Accession XM\_031009). Accordingly, utilities of VGAM1638 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90342. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1639 (VGAM1639) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55483] VGAM1639 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1639 was detected is described hereinabove with reference to Figs. 1–8.

[55484] VGAM1639 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1639 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55485] VGAM1639 gene encodes a VGAM1639 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1639 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1639 precursor RNA is designated SEQ ID:1625, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1625 is located at position 121407 relative to the genome of Human Herpesvirus 8.

[55486] VGAM1639 precursor RNA folds onto itself, forming VGAM1639 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55487] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1639 folded precursor RNA into VGAM1639 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1639 RNA is designated SEQ ID:4350, and is provided hereinbelow with reference to the sequence listing part.

[55488] VGAM1639 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1639 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1639 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[55489] VGAM1639 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1639 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1639 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1639 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1639 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55490] The complementary binding of VGAM1639 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1639 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1639 host target RNA into VGAM1639 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55491] It is appreciated that VGAM1639 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1639 host target genes. The mRNA of each one of this plurality of VGAM1639 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1639 RNA, herein designated VGAM RNA, and which when bound by VGAM1639 RNA causes inhibition of translation of respective one or more VGAM1639 host target proteins.

[55492] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1639 gene, herein designated VGAM GENE, on one or more VGAM1639 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55493] It is yet further appreciated that a function of VGAM1639 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1639 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1639 correlate with, and may be deduced from, the identity of the host target genes which VGAM1639 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55494] Nucleotide sequences of the VGAM1639 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1639 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1639 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1639 are further  
described hereinbelow with reference to Table 1.

[55495] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1639 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1639 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[55496] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1639 gene, herein designated VGAM is  
inhibition of expression of VGAM1639 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1639 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1639  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[55497] LOC114971 (Accession XM\_054936) is a VGAM1639 host  
target gene. LOC114971 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by LOC114971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114971 BINDING SITE, designated SEQ ID:36206, to the nucleotide sequence of VGAM1639 RNA, herein designated VGAM RNA, also designated SEQ ID:4350.

[55498] A function of VGAM1639 is therefore inhibition of LOC114971 (Accession XM\_054936). Accordingly, utilities of VGAM1639 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114971. LOC221773 (Accession XM\_165802) is another VGAM1639 host target gene. LOC221773 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221773 BINDING SITE, designated SEQ ID:43759, to the nucleotide sequence of VGAM1639 RNA, herein designated VGAM RNA, also designated SEQ ID:4350.

[55499] Another function of VGAM1639 is therefore inhibition of

LOC221773 (Accession XM\_165802). Accordingly, utilities of VGAM1639 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221773. LOC255533 (Accession XM\_173073) is another VGAM1639 host target gene. LOC255533 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255533, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255533 BINDING SITE, designated SEQ ID:46326, to the nucleotide sequence of VGAM1639 RNA, herein designated VGAM RNA, also designated SEQ ID:4350.

[55500] Another function of VGAM1639 is therefore inhibition of LOC255533 (Accession XM\_173073). Accordingly, utilities of VGAM1639 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255533. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1640 (VGAM1640) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[55501] VGAM1640 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1640 was detected is described hereinabove with reference to Figs. 1–8.

[55502] VGAM1640 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1640 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55503] VGAM1640 gene encodes a VGAM1640 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1640 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1640 precursor RNA is designated SEQ ID:1626, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1626 is located at position 117446 relative to the genome of Human Herpesvirus 8.

[55504] VGAM1640 precursor RNA folds onto itself, forming VGAM1640 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55505] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1640 folded precursor RNA into VGAM1640 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1640 RNA is designated SEQ ID:4351, and is provided hereinbelow with reference to the sequence listing part.

[55506] VGAM1640 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1640 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1640 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[55507] VGAM1640 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1640 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1640 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1640 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1640 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[55508] The complementary binding of VGAM1640 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1640 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1640 host target RNA into VGAM1640 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55509] It is appreciated that VGAM1640 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1640 host target genes. The mRNA of each one of this plurality of VGAM1640 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1640 RNA, herein designated VGAM RNA, and which when bound by VGAM1640 RNA causes inhibition of translation of respective one or more VGAM1640 host target proteins.

[55510] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1640 gene, herein designated VGAM GENE, on one

or more VGAM1640 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55511] It is yet further appreciated that a function of VGAM1640 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1640 correlate with, and may be deduced from, the identity of the host target genes which VGAM1640 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[55512] Nucleotide sequences of the VGAM1640 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1640 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1640 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1640 are further described hereinbelow with reference to Table 1.

[55513] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1640 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1640 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55514] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1640 gene, herein designated VGAM is inhibition of expression of VGAM1640 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1640 correlate with, and may be deduced from, the identity of the target genes which VGAM1640 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55515] Reticulon 3 (RTN3, Accession XM\_058207) is a VGAM1640

host target gene. RTN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RTN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RTN3 BINDING SITE, designated SEQ ID:36586, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55516] A function of VGAM1640 is therefore inhibition of Reticulon 3 (RTN3, Accession XM\_058207), a gene which is a member of the reticulon (neuroendocrine-specific, NSP) family. Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RTN3. The function of RTN3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM596. Tuftelin 1 (TUFT1, Accession NM\_020127) is another VGAM1640 host target gene. TUFT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUFT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUFT1 BINDING SITE, designated SEQ ID:21320, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55517] Another function of VGAM1640 is therefore inhibition of Tuftelin 1 (TUFT1, Accession NM\_020127), a gene which appears to play a role in cytokinesis, cell shape, and specialized functions such as secretion and capping. Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUFT1. The function of TUFT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1152. Chromosome 6 Open Reading Frame 33 (C6orf33, Accession NM\_133367) is another VGAM1640 host target gene. C6orf33 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf33 BINDING SITE, designated SEQ ID:28494, to the

nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55518] Another function of VGAM1640 is therefore inhibition of Chromosome 6 Open Reading Frame 33 (C6orf33, Accession NM\_133367). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf33. FLJ23191 (Accession NM\_024574) is another VGAM1640 host target gene. FLJ23191 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ23191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23191 BINDING SITE, designated SEQ ID:23805, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55519] Another function of VGAM1640 is therefore inhibition of FLJ23191 (Accession NM\_024574). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23191. FLJ30213 (Accession NM\_145008) is another VGAM1640 host target gene. FLJ30213 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30213 BINDING SITE, designated SEQ ID:29610, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55520] Another function of VGAM1640 is therefore inhibition of FLJ30213 (Accession NM\_145008). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30213. KIAA1184 (Accession NM\_022572) is another VGAM1640 host target gene. KIAA1184 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1184, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1184 BINDING SITE, designated SEQ ID:22898, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55521] Another function of VGAM1640 is therefore inhibition of

KIAA1184 (Accession NM\_022572). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1184. NDP52 (Accession NM\_005831) is another VGAM1640 host target gene. NDP52 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDP52, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDP52 BINDING SITE, designated SEQ ID:12442, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55522] Another function of VGAM1640 is therefore inhibition of NDP52 (Accession NM\_005831). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDP52. Trinucleotide Repeat Containing 6 (TNRC6, Accession XM\_047123) is another VGAM1640 host target gene. TNRC6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNRC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of TNRC6 BINDING SITE, designated SEQ ID:34901, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55523] Another function of VGAM1640 is therefore inhibition of Trinucleotide Repeat Containing 6 (TNRC6, Accession XM\_047123). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNRC6. LOC129676 (Accession XM\_065341) is another VGAM1640 host target gene. LOC129676 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC129676, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129676 BINDING SITE, designated SEQ ID:37287, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55524] Another function of VGAM1640 is therefore inhibition of LOC129676 (Accession XM\_065341). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC129676. LOC152905 (Accession XM\_017966) is another VGAM1640 host target gene. LOC152905 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152905, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152905 BINDING SITE, designated SEQ ID:30331, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55525] Another function of VGAM1640 is therefore inhibition of LOC152905 (Accession XM\_017966). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152905. LOC254402 (Accession XM\_174207) is another VGAM1640 host target gene. LOC254402 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254402, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254402 BINDING SITE, designated SEQ ID:46583, to



the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55526] Another function of VGAM1640 is therefore inhibition of LOC254402 (Accession XM\_174207). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254402. LOC56267 (Accession NM\_019610) is another VGAM1640 host target gene. LOC56267 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC56267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56267 BINDING SITE, designated SEQ ID:21230, to the nucleotide sequence of VGAM1640 RNA, herein designated VGAM RNA, also designated SEQ ID:4351.

[55527] Another function of VGAM1640 is therefore inhibition of LOC56267 (Accession NM\_019610). Accordingly, utilities of VGAM1640 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56267. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1641 (VGAM1641) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55528] VGAM1641 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1641 was detected is described hereinabove with reference to Figs. 1–8.

[55529] VGAM1641 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cell Fusing Agent Virus. VGAM1641 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55530] VGAM1641 gene encodes a VGAM1641 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1641 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1641 precursor RNA is designated SEQ ID:1627, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1627 is located at position 9147 relative to the genome of Cell Fusing Agent Virus.

[55531] VGAM1641 precursor RNA folds onto itself, forming VGAM1641 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55532] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1641 folded precursor RNA into VGAM1641 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1641 RNA is designated SEQ ID:4352, and is provided hereinbelow with reference to the sequence listing part.

[55533] VGAM1641 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1641 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1641 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[55534] VGAM1641 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1641 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1641 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1641 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1641 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55535] The complementary binding of VGAM1641 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1641 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1641 host target RNA into VGAM1641 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55536] It is appreciated that VGAM1641 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1641 host target genes. The mRNA of each one of this plurality of VGAM1641 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1641 RNA, herein designated VGAM RNA, and which when bound by VGAM1641 RNA causes inhibition of translation of respective one or more VGAM1641 host target proteins.

[55537] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1641 gene, herein designated VGAM GENE, on one or more VGAM1641 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55538] It is yet further appreciated that a function of VGAM1641 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1641 include diagnosis, prevention and treatment of viral infection by Cell Fusing Agent Virus. Specific functions, and accordingly utilities, of VGAM1641 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1641 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55539] Nucleotide sequences of the VGAM1641 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1641 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1641 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1641 are further described hereinbelow with reference to Table 1.

[55540] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1641 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1641 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55541] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1641 gene, herein designated VGAM is inhibition of expression of VGAM1641 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1641 correlate with, and may be deduced from, the identity of the target genes which VGAM1641

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55542] Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542) is a VGAM1641 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45219, to the nucleotide sequence of VGAM1641 RNA, herein designated VGAM RNA, also designated SEQ ID:4352.

[55543] A function of VGAM1641 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM1641 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. Fig. 1 further provides a conceptual descrip-



tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1642 (VGAM1642) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55544] VGAM1642 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1642 was detected is described hereinabove with reference to Figs. 1–8.

[55545] VGAM1642 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cell Fusing Agent Virus. VGAM1642 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55546] VGAM1642 gene encodes a VGAM1642 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1642 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1642 precursor RNA is designated SEQ ID:1628, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1628 is located at position 8550 relative to the genome of Cell Fusing Agent Virus.

[55547] VGAM1642 precursor RNA folds onto itself, forming VGAM1642 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55548] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1642 folded precursor RNA into VGAM1642 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1642 RNA is designated SEQ ID:4353, and is provided hereinbelow with reference to the sequence listing part.

[55549] VGAM1642 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1642 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1642 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[55550] VGAM1642 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1642 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1642 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1642 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1642 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[55551] The complementary binding of VGAM1642 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1642 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1642 host target RNA into VGAM1642 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55552] It is appreciated that VGAM1642 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1642 host target genes. The mRNA of each one of this plurality of VGAM1642 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1642 RNA, herein designated VGAM RNA, and which when bound by VGAM1642 RNA causes inhibition of translation of respective one or more

VGAM1642 host target proteins.

[55553] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1642 gene, herein designated VGAM GENE, on one or more VGAM1642 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55554] It is yet further appreciated that a function of VGAM1642 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1642 include diagnosis, prevention and treatment of viral infection by Cell Fusing Agent Virus.

Specific functions, and accordingly utilities, of VGAM1642 correlate with, and may be deduced from, the identity of the host target genes which VGAM1642 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55555] Nucleotide sequences of the VGAM1642 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1642 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1642 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1642 are further described hereinbelow with reference to Table 1.

[55556] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1642 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1642 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55557] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1642 gene, herein designated VGAM is inhibition of expression of VGAM1642 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1642 correlate with, and may be deduced from, the identity of the target genes which VGAM1642 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55558] LOC254122 (Accession XM\_170660) is a VGAM1642 host target gene. LOC254122 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254122 BINDING SITE, designated SEQ ID:45437, to the nucleotide sequence of VGAM1642 RNA, herein designated VGAM RNA, also designated SEQ ID:4353.

[55559] A function of VGAM1642 is therefore inhibition of LOC254122 (Accession XM\_170660). Accordingly, utilities of VGAM1642 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254122. LOC254830 (Accession XM\_175118) is another VGAM1642 host target gene. LOC254830 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254830, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254830 BINDING SITE, designated SEQ ID:46612, to the nucleotide sequence of VGAM1642 RNA, herein designated VGAM RNA, also designated SEQ ID:4353.

[55560] Another function of VGAM1642 is therefore inhibition of LOC254830 (Accession XM\_175118). Accordingly, utilities of VGAM1642 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254830. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1643 (VGAM1643) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55561] VGAM1643 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1643 was detected is described hereinabove with reference to Figs. 1-8.

[55562] VGAM1643 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cell Fusing Agent Virus. VGAM1643 host target gene, herein designated VGAM



HOST TARGET GENE, is a human gene contained in the human genome.

[55563] VGAM1643 gene encodes a VGAM1643 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1643 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1643 precursor RNA is designated SEQ ID:1629, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1629 is located at position 1340 relative to the genome of Cell Fusing Agent Virus.

[55564] VGAM1643 precursor RNA folds onto itself, forming VGAM1643 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55565] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1643 folded precursor RNA into VGAM1643

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1643 RNA is designated SEQ ID:4354, and is provided hereinbelow with reference to the sequence listing part.

[55566] VGAM1643 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1643 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1643 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55567] VGAM1643 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1643 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1643 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1643 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1643 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55568] The complementary binding of VGAM1643 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1643 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1643 host target RNA into VGAM1643 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[55569] It is appreciated that VGAM1643 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1643 host target genes. The mRNA of each one of this plurality of VGAM1643 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1643 RNA, herein designated VGAM RNA, and which when bound by VGAM1643 RNA causes inhibition of translation of respective one or more VGAM1643 host target proteins.

[55570] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1643 gene, herein designated VGAM GENE, on one or more VGAM1643 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55571] It is yet further appreciated that a function of VGAM1643 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1643 include diagnosis, prevention and treatment of viral infection by Cell Fusing Agent Virus. Specific functions, and accordingly utilities, of VGAM1643 correlate with, and may be deduced from, the identity of the host target genes which VGAM1643 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55572] Nucleotide sequences of the VGAM1643 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1643 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1643 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1643 are further described hereinbelow with reference to Table 1.

[55573] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1643 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1643 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55574] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1643 gene, herein designated VGAM is inhibition of expression of VGAM1643 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1643 correlate with, and may be deduced from, the identity of the target genes which VGAM1643 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55575] GNAS Complex Locus (GNAS, Accession NM\_016592) is a VGAM1643 host target gene. GNAS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAS BINDING SITE, designated SEQ ID:18676, to the nucleotide sequence of VGAM1643 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4354.

[55576] A function of VGAM1643 is therefore inhibition of GNAS Complex Locus (GNAS, Accession NM\_016592), a gene which transduces signals from G protein-coupled receptors and activates adenylyl cyclase. Accordingly, utilities of VGAM1643 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAS. The function of GNAS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1205. Zinc Finger Protein 43 (HTF6) (ZNF43, Accession NM\_003423) is another VGAM1643 host target gene. ZNF43 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF43, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF43 BINDING SITE, designated SEQ ID:9470, to the nucleotide sequence of VGAM1643 RNA, herein designated VGAM RNA, also designated SEQ ID:4354.

[55577] Another function of VGAM1643 is therefore inhibition of Zinc Finger Protein 43 (HTF6) (ZNF43, Accession

NM\_003423), a gene which may be involved in transcriptional regulation. Accordingly, utilities of VGAM1643 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF43. The function of ZNF43 has been established by previous studies. By screening a cDNA library derived from a human undifferentiated embryonal carcinoma cell line with the coding sequence of the ZNF85 (OMIM Ref. No. 603899) N-terminal nonfinger region, which spans the KRAB domain, Bellefroid et al. (1991) isolated cDNAs encoding 11 distinct KRAB ZNFs, including ZNF43, which they called HTF6. Lovering and Trowsdale (1991) noted that this HTF6 cDNA, which differs from the 2 ZNF43 cDNAs that they isolated, encodes a ZNF lacking the KRAB A box. Bellefroid et al. (1993) reported the characterization of a subgroup of KRAB ZNFs, named the ZNF91 family, of which ZNF43 is a member. These proteins contain a conserved linker region, called the ZNF91-related spacer region, between their N-terminal KRAB domain and their first finger unit. The authors found that members of the ZNF91 family are widely expressed in human tissues, with the highest expression in T-lymphoid cells.

[55578] Full details of the abovementioned studies are described



in the following publications, the disclosure of which are hereby incorporated by reference:

[55579] Lovering, R.; Trowsdale, J. : A gene encoding 22 highly related zinc fingers is expressed in lymphoid cell lines. *Nucleic Acids Res.* 19: 2921–2928, 1991. ; and

[55580] Bellefroid, E. J.; Poncelet, D. A.; Lecocq, P. J.; Revelant, O.; Martial, J. A. : The evolutionarily conserved Kruppel-associated box domain defines a subfamily of eukaryotic multifingered.

[55581] Further studies establishing the function and utilities of ZNF43 are found in John Hopkins OMIM database record ID 603972, and in cited publications numbered 7425–742 and 7466 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Leptin Receptor Overlapping Transcript-like 1 (LEPROTL1, Accession NM\_015344) is another VGAM1643 host target gene. LEPROTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEPROTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEPROTL1 BINDING SITE, designated SEQ ID:17650, to the nucleotide sequence of VGAM1643 RNA,

herein designated VGAM RNA, also designated SEQ ID:4354.

[55582] Another function of VGAM1643 is therefore inhibition of Leptin Receptor Overlapping Transcript-like 1 (LEPROTL1, Accession NM\_015344). Accordingly, utilities of VGAM1643 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEP-ROTL1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1644 (VGAM1644) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55583] VGAM1644 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1644 was detected is described hereinabove with reference to Figs. 1-8.

[55584] VGAM1644 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Dengue Virus. VGAM1644 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55585] VGAM1644 gene encodes a VGAM1644 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1644 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1644 precursor RNA is designated SEQ ID:1630, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1630 is located at position 10625 relative to the genome of Dengue Virus.

[55586] VGAM1644 precursor RNA folds onto itself, forming VGAM1644 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55587] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1644 folded precursor RNA into VGAM1644 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM1644 RNA is designated SEQ ID:4355, and is provided hereinbelow with reference to the sequence listing part.

[55588] VGAM1644 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1644 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1644 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55589] VGAM1644 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1644 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1644 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1644 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1644 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55590] The complementary binding of VGAM1644 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1644 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1644 host target RNA into VGAM1644 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55591] It is appreciated that VGAM1644 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1644 host target genes. The mRNA of each one of this plurality of VGAM1644 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1644 RNA, herein designated VGAM RNA, and which when bound by VGAM1644 RNA causes inhibition of translation of respective one or more VGAM1644 host target proteins.

[55592] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1644 gene, herein designated VGAM GENE, on one or more VGAM1644 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[55593] It is yet further appreciated that a function of VGAM1644 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of viral infection by Dengue Virus. Specific functions, and accordingly utilities, of VGAM1644 correlate with, and may be deduced from, the identity of the host target genes which VGAM1644 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55594] Nucleotide sequences of the VGAM1644 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1644 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1644 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1644 are further described hereinbelow with reference to Table 1.

[55595] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1644 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1644 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55596] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1644 gene, herein designated VGAM is inhibition of expression of VGAM1644 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1644 correlate with, and may be deduced from, the identity of the target genes which VGAM1644 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55597] A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 5 (aggrecanase-2) (ADAMTS5, Accession NM\_007038) is a VGAM1644 host target gene. ADAMTS5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAMTS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS5 BINDING SITE, designated SEQ ID:13918, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also des-



ignated SEQ ID:4355.

[55598] A function of VGAM1644 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 5 (aggrecanase-2) (ADAMTS5, Accession NM\_007038), a gene which cleaves aggrecan, a cartilage proteoglycan, and may be involved in its turnover. Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS5. The function of ADAMTS5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM35. Alkaline Phosphatase, Intestinal (ALPI, Accession NM\_001631) is another VGAM1644 host target gene. ALPI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALPI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALPI BINDING SITE, designated SEQ ID:7345, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55599] Another function of VGAM1644 is therefore inhibition of

Alkaline Phosphatase, Intestinal (ALPI, Accession NM\_001631), a gene which is a glycoprotein phosphatase. Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALPI. The function of ALPI and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM885. Dual Specificity Phosphatase 2 (DUSP2, Accession NM\_004418) is another VGAM1644 host target gene. DUSP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DUSP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP2 BINDING SITE, designated SEQ ID:10682, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55600] Another function of VGAM1644 is therefore inhibition of Dual Specificity Phosphatase 2 (DUSP2, Accession NM\_004418), a gene which regulates mitogenic signal transduction. Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with DUSP2. The function of DUSP2 has been established by previous studies. Mitogenic stimulation of quiescent cells leads to the rapid and reversible activation of mitogen-activated protein (MAP) kinases via dual phosphorylation within a thr-glu-tyr motif. Following activation, MAP kinases translocate into the nucleus where they phosphorylate several signal transduction targets. The dual-specificity phosphatases can reverse MAP kinase activation by dephosphorylating phosphotyrosine and phosphothreonine residues. Rohan et al. (1993) isolated mouse and human cDNAs encoding PAC1, a mitogen-induced 32-kD protein that contains a sequence that is associated with enzymatic activity in previously identified protein phosphotyrosine phosphatases. The predicted human PAC1 protein has 314 amino acids. Northern blot analysis of human cell lines and mouse tissues revealed that PAC1 is expressed predominantly in hematopoietic tissues. By immunofluorescence of transfected cells and mitogen-stimulated T cells, Rohan et al. (1993) localized PAC1 to the nucleus. Ward et al. (1994) demonstrated that PAC1 is a dual-specific thr/tyr phosphatase that is a physiologically relevant MAP kinase phosphatase. Yi et al. (1995) determined that the PAC1, or

DUSP2, gene contains 4 exons that span approximately 2.3 kb. By somatic cell hybrid analysis, linkage analysis, and in situ hybridization, Yi et al. (1995) mapped the PAC1 gene to 2p11.2–q11. Using fluorescence in situ hybridization, Martell et al. (1994) refined the localization of the PAC1 gene to 2q11.

[55601] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55602] Rohan, P. J.; Davis, P.; Moskaluk, C. A.; Kearns, M.; Krutzsch, H.; Siebenlist, U.; Kelly, K. : PAC–1: a mitogen–induced nuclear protein tyrosine phosphatase. Science 259: 1763–1766, 1993. ; and

[55603] Yi, H.; Morton, C. C.; Weremowicz, S.; McBride, O. W.; Kelly, K. : Genomic organization and chromosomal localization of the DUSP2 gene, encoding a MAP kinase phosphatase, to human 2p11.

[55604] Further studies establishing the function and utilities of DUSP2 are found in John Hopkins OMIM database record ID 603068, and in cited publications numbered 10055–8849 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.FK506 Binding Protein 1B, 12.6 KDa (FKBP1B, Acces–

sion NM\_054033) is another VGAM1644 host target gene. FKBP1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FKBP1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKBP1B BINDING SITE, designated SEQ ID:27643, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55605] Another function of VGAM1644 is therefore inhibition of FK506 Binding Protein 1B, 12.6 KDa (FKBP1B, Accession NM\_054033), a gene which may play a unique physiological role in excitation-contraction coupling in cardiac muscle. Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKBP1B. The function of FKBP1B has been established by previous studies. Arakawa et al. (1994) isolated a novel gene encoding a protein closely related to the human FK506-binding proteins from a human fetal brain cDNA library. The full-length cDNA encoded an open reading frame of 108 amino acids with 88% identity in predicted amino acid sequence to FKBP12

(OMIM Ref. No. 186945). The FKBP1L gene, designated OTK4 by the authors, also had sequence similarity with other FKBP's in species ranging from prokaryotes to humans, including FKPB13 (OMIM Ref. No. 186946), FKBP25 (OMIM Ref. No. 186947), and FKBP52 (OMIM Ref. No. 600611). Recombinant FKBP1L protein produced in *E. coli* showed peptidyl-prolyl cis-trans isomerase activity like that of other FKBP's. The authors also found an alternatively spliced transcript that contained a 45-bp insertion which included a stop codon. Both transcripts were ubiquitously expressed in several human tissues examined by RT-PCR. The International Radiation Hybrid Mapping Consortium mapped the FKBP1B gene to chromosome 2 (SHGC-31628). Animal model experiments lend further support to the function of FKBP1B. Xin et al. (2002) generated mice deficient in FKBP12.6 by targeted disruption. Male mutant mice had cardiac hypertrophy, but not females.

[55606] It is appreciated that the abovementioned animal model for FKBP1B is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[55607] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [55608] Arakawa, H.; Nagase, H.; Hayashi, N.; Fujiwara, T.; Ogawa, M.; Shin, S.; Nakamura, Y. : Molecular cloning and expression of a novel human gene that is highly homologous to human FK506-binding protein 12kDa (hFKBP-12) and characterization of two alternatively spliced transcripts. Biochem. Biophys. Res. Commun. 200: 836-843, 1994. ; and
- [55609] Xin, H.-B.; Senbonmatsu, T.; Cheng, D.-S.; Wang, Y.-X. Copello, J. A.; Ji, G.-J.; Collier, M. L.; Deng, K.-Y.; Jeyakumar, L. H.; Magnuson, M. A.; Inagami, T.; Kotlikoff, M. I.; Fleische.
- [55610] Further studies establishing the function and utilities of FKBP1B are found in John Hopkins OMIM database record ID 600620, and in cited publications numbered 6560-6561 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Homeo Box B6 (HOXB6, Accession XM\_008560) is another VGAM1644 host target gene. HOXB6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXB6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXB6 BINDING SITE, designated SEQ ID:30088, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55611] Another function of VGAM1644 is therefore inhibition of Homeo Box B6 (HOXB6, Accession XM\_008560), a gene which participates in establishing segmentation patterns and in determining segment identities. Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXB6. The function of HOXB6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1355. Kinesin Family Member 5C (KIF5C, Accession NM\_004522) is another VGAM1644 host target gene. KIF5C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF5C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF5C BINDING SITE, designated SEQ ID:10858, to the nucleotide sequence of VGAM1644 RNA,



herein designated VGAM RNA, also designated SEQ ID:4355.

[55612] Another function of VGAM1644 is therefore inhibition of Kinesin Family Member 5C (KIF5C, Accession NM\_004522). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF5C. Leucine Zipper Transcription Factor-like 1 (LZTFL1, Accession NM\_020347) is another VGAM1644 host target gene. LZTFL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LZTFL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTFL1 BINDING SITE, designated SEQ ID:21599, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55613] Another function of VGAM1644 is therefore inhibition of Leucine Zipper Transcription Factor-like 1 (LZTFL1, Accession NM\_020347). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTFL1. Phosphatidylinositol Glycan, Class A (paroxysmal nocturnal

hemoglobinuria) (PIGA, Accession NM\_020472) is another VGAM1644 host target gene. PIGA BINDING SITE1 through PIGA BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PIGA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIGA BINDING SITE1 through PIGA BINDING SITE3, designated SEQ ID:21713, SEQ ID:21720 and SEQ ID:8500 respectively, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55614] Another function of VGAM1644 is therefore inhibition of Phosphatidylinositol Glycan, Class A (paroxysmal nocturnal hemoglobinuria) (PIGA, Accession NM\_020472). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIGA. Syntaxin Binding Protein 1 (STXBP1, Accession NM\_003165) is another VGAM1644 host target gene. STXBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STXBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of STXBP1 BINDING SITE, designated SEQ ID:9143, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55615] Another function of VGAM1644 is therefore inhibition of Syntaxin Binding Protein 1 (STXBP1, Accession NM\_003165), a gene which may play a role in determining the specificity of intracellular fusion reactions. Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STXBP1. The function of STXBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM708. Transcription Factor Binding to IGHM Enhancer 3 (TFE3, Accession NM\_006521) is another VGAM1644 host target gene. TFE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFE3 BINDING SITE, designated SEQ ID:13277, to the nucleotide

sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55616] Another function of VGAM1644 is therefore inhibition of Transcription Factor Binding to IGHM Enhancer 3 (TFE3, Accession NM\_006521), a gene which is a positive-acting transcription factor that binds to the immunoglobulin enhancer mue3 motif. Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFE3. The function of TFE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM443. Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM\_021083) is another VGAM1644 host target gene. XK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XK BINDING SITE, designated SEQ ID:22058, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55617] Another function of VGAM1644 is therefore inhibition of

Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM\_021083). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XK. Apolipoprotein A-V (APOA5, Accession NM\_052968) is another VGAM1644 host target gene. APOA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOA5 BINDING SITE, designated SEQ ID:27539, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55618] Another function of VGAM1644 is therefore inhibition of Apolipoprotein A-V (APOA5, Accession NM\_052968). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOA5. BANP (Accession XM\_038696) is another VGAM1644 host target gene. BANP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BANP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BANP BINDING SITE, designated SEQ ID:32913, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55619] Another function of VGAM1644 is therefore inhibition of BANP (Accession XM\_038696). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BANP. CD109 (Accession NM\_133493) is another VGAM1644 host target gene. CD109 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD109, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD109 BINDING SITE, designated SEQ ID:28573, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55620] Another function of VGAM1644 is therefore inhibition of CD109 (Accession NM\_133493). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD109.

Cleavage and Polyadenylation Specific Factor 2, 100kDa (CPSF2, Accession XM\_029311) is another VGAM1644 host target gene. CPSF2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CPSF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPSF2 BINDING SITE, designated SEQ ID:30866, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55621] Another function of VGAM1644 is therefore inhibition of Cleavage and Polyadenylation Specific Factor 2, 100kDa (CPSF2, Accession XM\_029311). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPSF2. FLJ12057 (Accession NM\_024768) is another VGAM1644 host target gene. FLJ12057 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12057 BINDING SITE,

designated SEQ ID:24126, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55622] Another function of VGAM1644 is therefore inhibition of FLJ12057 (Accession NM\_024768). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12057. FLJ20203 (Accession NM\_017710) is another VGAM1644 host target gene. FLJ20203 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20203, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20203 BINDING SITE, designated SEQ ID:19291, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55623] Another function of VGAM1644 is therefore inhibition of FLJ20203 (Accession NM\_017710). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20203. FLJ20508 (Accession NM\_017850) is another VGAM1644 host target gene. FLJ20508 BINDING SITE is



HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20508 BINDING SITE, designated SEQ ID:19518, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55624] Another function of VGAM1644 is therefore inhibition of FLJ20508 (Accession NM\_017850). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20508. FLJ21140 (Accession NM\_024776) is another VGAM1644 host target gene. FLJ21140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21140 BINDING SITE, designated SEQ ID:24142, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55625] Another function of VGAM1644 is therefore inhibition of

FLJ21140 (Accession NM\_024776). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21140. FLJ21459 (Accession NM\_024521) is another VGAM1644 host target gene. FLJ21459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21459 BINDING SITE, designated SEQ ID:23719, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55626] Another function of VGAM1644 is therefore inhibition of FLJ21459 (Accession NM\_024521). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21459. Gamma-aminobutyric Acid (GABA) B Receptor, 1 (GABBR1, Accession NM\_001470) is another VGAM1644 host target gene. GABBR1 BINDING SITE1 and GABBR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GABBR1, corresponding to HOST TARGET binding sites such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABBR1 BINDING SITE1 and GABBR1 BINDING SITE2, designated SEQ ID:7206 and SEQ ID:22423 respectively, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55627] Another function of VGAM1644 is therefore inhibition of Gamma-aminobutyric Acid (GABA) B Receptor, 1 (GABBR1, Accession NM\_001470). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABBR1. KIAA1023 (Accession NM\_017604) is another VGAM1644 host target gene. KIAA1023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1023 BINDING SITE, designated SEQ ID:19093, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55628] Another function of VGAM1644 is therefore inhibition of KIAA1023 (Accession NM\_017604). Accordingly, utilities

of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1023. KIAA1317 (Accession XM\_098368) is another VGAM1644 host target gene. KIAA1317 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1317 BINDING SITE, designated SEQ ID:41632, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55629] Another function of VGAM1644 is therefore inhibition of KIAA1317 (Accession XM\_098368). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1317. KIAA1617 (Accession XM\_166140) is another VGAM1644 host target gene. KIAA1617 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1617 BINDING SITE, designated SEQ ID:43942, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55630] Another function of VGAM1644 is therefore inhibition of KIAA1617 (Accession XM\_166140). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1617. MGC10966 (Accession NM\_031471) is another VGAM1644 host target gene. MGC10966 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC10966, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10966 BINDING SITE, designated SEQ ID:25538, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55631] Another function of VGAM1644 is therefore inhibition of MGC10966 (Accession NM\_031471). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10966. Nuclear Receptor Subfamily 6, Group A, Member 1 (NR6A1, Accession NM\_033335) is another

VGAM1644 host target gene. NR6A1 BINDING SITE1 through NR6A1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NR6A1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR6A1 BINDING SITE1 through NR6A1 BINDING SITE3, designated SEQ ID:27189, SEQ ID:27183 and SEQ ID:7235 respectively, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55632] Another function of VGAM1644 is therefore inhibition of Nuclear Receptor Subfamily 6, Group A, Member 1 (NR6A1, Accession NM\_033335). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR6A1. PME-1 (Accession NM\_016147) is another VGAM1644 host target gene. PME-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PME-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PME-1 BINDING SITE, des-

ignated SEQ ID:18231, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55633] Another function of VGAM1644 is therefore inhibition of PME-1 (Accession NM\_016147). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PME-1. Solute Carrier Family 38, Member 4 (SLC38A4, Accession NM\_018018) is another VGAM1644 host target gene. SLC38A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC38A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC38A4 BINDING SITE, designated SEQ ID:19759, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55634] Another function of VGAM1644 is therefore inhibition of Solute Carrier Family 38, Member 4 (SLC38A4, Accession NM\_018018). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC38A4. LOC145739

(Accession XM\_085222) is another VGAM1644 host target gene. LOC145739 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145739 BINDING SITE, designated SEQ ID:37961, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55635] Another function of VGAM1644 is therefore inhibition of LOC145739 (Accession XM\_085222). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145739. LOC147180 (Accession XM\_097207) is another VGAM1644 host target gene. LOC147180 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147180, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147180 BINDING SITE, designated SEQ ID:40818, to the nucleotide sequence of VGAM1644 RNA, herein design-



nated VGAM RNA, also designated SEQ ID:4355.

[55636] Another function of VGAM1644 is therefore inhibition of LOC147180 (Accession XM\_097207). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147180. LOC148293 (Accession XM\_086138) is another VGAM1644 host target gene. LOC148293 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148293, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148293 BINDING SITE, designated SEQ ID:38519, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55637] Another function of VGAM1644 is therefore inhibition of LOC148293 (Accession XM\_086138). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148293. LOC149535 (Accession XM\_086567) is another VGAM1644 host target gene. LOC149535 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149535, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149535 BINDING SITE, designated SEQ ID:38772, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55638] Another function of VGAM1644 is therefore inhibition of LOC149535 (Accession XM\_086567). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149535. LOC150343 (Accession XM\_086823) is another VGAM1644 host target gene. LOC150343 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150343, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150343 BINDING SITE, designated SEQ ID:38903, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55639] Another function of VGAM1644 is therefore inhibition of LOC150343 (Accession XM\_086823). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC150343. LOC152048 (Accession XM\_098158) is another VGAM1644 host target gene. LOC152048 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152048, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152048 BINDING SITE, designated SEQ ID:41426, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55640] Another function of VGAM1644 is therefore inhibition of LOC152048 (Accession XM\_098158). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152048. LOC155179 (Accession XM\_088169) is another VGAM1644 host target gene. LOC155179 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC155179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155179 BINDING SITE, designated SEQ ID:39559, to

the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55641] Another function of VGAM1644 is therefore inhibition of LOC155179 (Accession XM\_088169). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155179. LOC221466 (Accession XM\_168087) is another VGAM1644 host target gene. LOC221466 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221466 BINDING SITE, designated SEQ ID:44994, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55642] Another function of VGAM1644 is therefore inhibition of LOC221466 (Accession XM\_168087). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221466. LOC255779 (Accession XM\_171147) is another VGAM1644 host target gene. LOC255779 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC255779, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255779 BINDING SITE, designated SEQ ID:45943, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55643] Another function of VGAM1644 is therefore inhibition of LOC255779 (Accession XM\_171147). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255779. LOC90049 (Accession XM\_028387) is another VGAM1644 host target gene. LOC90049 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90049, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90049 BINDING SITE, designated SEQ ID:30698, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55644] Another function of VGAM1644 is therefore inhibition of LOC90049 (Accession XM\_028387). Accordingly, utilities

of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90049. LOC91252 (Accession XM\_037173) is another VGAM1644 host target gene. LOC91252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91252 BINDING SITE, designated SEQ ID:32553, to the nucleotide sequence of VGAM1644 RNA, herein designated VGAM RNA, also designated SEQ ID:4355.

[55645] Another function of VGAM1644 is therefore inhibition of LOC91252 (Accession XM\_037173). Accordingly, utilities of VGAM1644 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91252. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1645 (VGAM1645) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55646] VGAM1645 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1645 was detected is described hereinabove with reference to Figs. 1–8.

[55647] VGAM1645 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Dengue Virus. VGAM1645 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55648] VGAM1645 gene encodes a VGAM1645 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1645 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1645 precursor RNA is designated SEQ ID:1631, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1631 is located at position 5184 relative to the genome of Dengue Virus.

[55649] VGAM1645 precursor RNA folds onto itself, forming VGAM1645 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55650] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1645 folded precursor RNA into VGAM1645 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1645 RNA is designated SEQ ID:4356, and is provided hereinbelow with reference to the sequence listing part.

[55651] VGAM1645 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1645 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1645 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated



5`UTR, PROTEIN CODING and 3`UTR respectively.

[55652] VGAM1645 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1645 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1645 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1645 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1645 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55653] The complementary binding of VGAM1645 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1645 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1645 host target RNA into VGAM1645 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55654] It is appreciated that VGAM1645 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1645 host target genes. The mRNA of each one of this plurality of VGAM1645 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1645 RNA, herein designated VGAM RNA, and which when bound by VGAM1645 RNA causes inhibition of translation of respective one or more VGAM1645 host target proteins.

[55655] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1645 gene, herein designated VGAM GENE, on one or more VGAM1645 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55656] It is yet further appreciated that a function of VGAM1645 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1645 include diagnosis, prevention and treatment of viral infection by Dengue Virus. Specific functions, and accordingly utilities, of VGAM1645 correlate with, and may be deduced from, the identity of the host target genes which VGAM1645 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55657] Nucleotide sequences of the VGAM1645 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1645 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1645 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1645 are further  
described hereinbelow with reference to Table 1.

[55658] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1645 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1645 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[55659] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1645 gene, herein designated VGAM is  
inhibition of expression of VGAM1645 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1645 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1645  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[55660] Collagen, Type IV, Alpha 1 (COL4A1, Accession  
NM\_001845) is a VGAM1645 host target gene. COL4A1

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL4A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A1 BINDING SITE, designated SEQ ID:7578, to the nucleotide sequence of VGAM1645 RNA, herein designated VGAM RNA, also designated SEQ ID:4356.

[55661] A function of VGAM1645 is therefore inhibition of Collagen, Type IV, Alpha 1 (COL4A1, Accession NM\_001845), a gene which is a member of a subfamily of collagen extracellular matrix proteins. Accordingly, utilities of VGAM1645 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A1. The function of COL4A1 has been established by previous studies. Types I, II, and III collagen, the so-called interstitial collagens, are in many ways distinct from basement membrane collagen. Type IV collagen does not form ordered fibrillar structures; rather, a meshwork is formed by 4 molecules held together at the ends. Both disulfide and typical lysyl-derived collagen crosslinks are involved (Kuhn, 1982). Crouch et al. (1980) presented evidence

that type IV procollagen contains 2 distinct chains. The collagen IV molecule is a heterotrimer of 2 alpha-1 chains and 1 alpha-2 chain (Mayne et al., 1984). There are presumably 2 gene loci responsible for the alpha-1 and alpha-2 chains of type IV collagen. Using a cloned gene as a probe on Southern blots of DNA from a panel of interspecies somatic cell hybrids, Solomon et al. (1985) assigned one of the collagen IV genes, COL4A1, to chromosome 13. Pihlajaniemi et al. (1985) used dual-laser sorted chromosomes and spot-blot analysis to assign genomic DNA sequences coding for COL4A1 to chromosome 13. By in situ hybridization, Boyd et al. (1986) localized the gene to the end of the long arm of chromosome 13. Southern and spot-blot hybridization showed that these genomic sequences were present only once per haploid genome. Emanuel et al. (1986) assigned COL4A1 to the telomeric region of 13q (13q34) by in situ hybridization. Bowcock et al. (1987) found that the COL4A1 locus is linked to D13S3, which in turn has been assigned to 13q33-q34 by in situ hybridization. They found a maximum lod score of 16.5 at  $\theta = 0.01$ . Griffin et al. (1987) showed by in situ hybridization and Southern blot analysis of DNA from somatic cell hybrids that the COL4A2 gene is also on the

distal long arm of chromosome 13, apparently closely linked to the alpha-1(IV) gene. By means of pulsed-field gel electrophoresis (PFGE) and infrequently cutting restriction enzymes, Cutting et al. (1987) showed that the COL4A1 and COL4A2 genes are separated by no more than 400 kb. Using RFLPs identified within the two genes, Hebert et al. (1987) also showed that COL4A1 and COL4A2 are closely linked. Bowcock et al. (1988) found that the COL4A1 and COL4A2 genes are linked, with a maximum likelihood estimate of recombination of 0.028 at a lod score of 19.98. This and the lack of linkage disequilibrium are inconsistent with relatively high recombination between the 2 loci--higher than expected for 2 genes that lie within 650 kb of each other. Koizumi et al. (1995) used interspecific and intersubspecific mapping panels to locate the Col4a1 gene to the centromeric region of mouse chromosome 8. COL4A2 (OMIM Ref. No. 120090) and coagulation factor X (F10; 227600) mapped to the same region, thus defining a new region of homology of synteny between mouse chromosome 8 and human chromosome 13 Goodpasture syndrome (glomerulonephritis and pulmonary hemorrhage). Butkowski et al. (1987) localized the Goodpasture epitope

to a novel chain of type IV collagen composed of 3 distinctive subunits--M1, M2\*, and M3. The Goodpasture epitope was found to be situated exclusively on M2\*.

Turner et al. (1992) demonstrated that the Goodpasture antigen is the alpha-3 chain of type IV collagen (COL4A3; 120070

[55662] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55663] Pihlajaniemi, T.; Tryggvason, K.; Myers, J. C.; Kurkinen, M.; Lebo, R.; Cheung, M.-C.; Prockop, D. J.; Boyd, C. D. : cDNA clones coding for the pro-alpha-1(IV) chain of human type IV procollagen reveal an unusual homology of amino acid sequences in two halves of the carboxyl terminal domain. J. Biol. Chem. 260: 7681-7687, 1985. ; and

[55664] Turner, N.; Mason, P. J.; Brown, R.; Fox, M.; Povey, S.; Rees, A.; Pusey, C. D. : Molecular cloning of the human Goodpasture antigen demonstrates it to be the alpha-3 chain of type IV c.

[55665] Further studies establishing the function and utilities of COL4A1 are found in John Hopkins OMIM database record ID 120130, and in cited publications numbered 266-270, 346-274, 4586, 3621-282, 383, 40 and 8951-406 listed



in the bibliography section hereinbelow, which are also hereby incorporated by reference. Follistatin-like 1 (FSTL1, Accession NM\_007085) is another VGAM1645 host target gene. FSTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FSTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FSTL1 BINDING SITE, designated SEQ ID:13947, to the nucleotide sequence of VGAM1645 RNA, herein designated VGAM RNA, also designated SEQ ID:4356.

[55666] Another function of VGAM1645 is therefore inhibition of Follistatin-like 1 (FSTL1, Accession NM\_007085), a gene which may modulate the action of some growth factors on cell proliferation and differentiation. Accordingly, utilities of VGAM1645 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FSTL1. The function of FSTL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM791. Membrane Component, Chromosome 11, Surface Marker 1 (M11S1, Accession NM\_005898) is another VGAM1645 host target gene. M11S1 BINDING SITE

is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by M11S1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of M11S1 BINDING SITE, designated SEQ ID:12518, to the nucleotide sequence of VGAM1645 RNA, herein designated VGAM RNA, also designated SEQ ID:4356.

[55667] Another function of VGAM1645 is therefore inhibition of Membrane Component, Chromosome 11, Surface Marker 1 (M11S1, Accession NM\_005898), a gene which may play a role in transporting nutrients from the gut lumen across the gutlining epithelial cell layer. Accordingly, utilities of VGAM1645 include diagnosis, prevention and treatment of diseases and clinical conditions associated with M11S1. The function of M11S1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM131. Zinc Finger Protein 124 (HZF-16) (ZNF124, Accession NM\_003431) is another VGAM1645 host target gene. ZNF124 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF124, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF124 BINDING SITE, designated SEQ ID:9481, to the nucleotide sequence of VGAM1645 RNA, herein designated VGAM RNA, also designated SEQ ID:4356.

[55668] Another function of VGAM1645 is therefore inhibition of Zinc Finger Protein 124 (HZF-16) (ZNF124, Accession NM\_003431). Accordingly, utilities of VGAM1645 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF124. DKFZP434O047 (Accession NM\_015594) is another VGAM1645 host target gene. DKFZP434O047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434O047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434O047 BINDING SITE, designated SEQ ID:17865, to the nucleotide sequence of VGAM1645 RNA, herein designated VGAM RNA, also designated SEQ ID:4356.

[55669] Another function of VGAM1645 is therefore inhibition of DKFZP434O047 (Accession NM\_015594). Accordingly,

utilities of VGAM1645 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434O047. FXYD Domain Containing Ion Transport Regulator 3 (FXYD3, Accession NM\_021910) is another VGAM1645 host target gene. FXYD3 BINDING SITE1 and FXYD3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FXYD3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FXYD3 BINDING SITE1 and FXYD3 BINDING SITE2, designated SEQ ID:22435 and SEQ ID:12592 respectively, to the nucleotide sequence of VGAM1645 RNA, herein designated VGAM RNA, also designated SEQ ID:4356.

[55670] Another function of VGAM1645 is therefore inhibition of FXYD Domain Containing Ion Transport Regulator 3 (FXYD3, Accession NM\_021910). Accordingly, utilities of VGAM1645 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FXYD3. RNA Binding Motif Protein 11 (RBM11, Accession NM\_144770) is another VGAM1645 host target gene. RBM11 BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by RBM11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBM11 BINDING SITE, designated SEQ ID:29560, to the nucleotide sequence of VGAM1645 RNA, herein designated VGAM RNA, also designated SEQ ID:4356.

[55671] Another function of VGAM1645 is therefore inhibition of RNA Binding Motif Protein 11 (RBM11, Accession NM\_144770). Accordingly, utilities of VGAM1645 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBM11. LOC203292 (Accession XM\_117527) is another VGAM1645 host target gene. LOC203292 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC203292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203292 BINDING SITE, designated SEQ ID:43500, to the nucleotide sequence of VGAM1645 RNA, herein designated VGAM RNA, also designated SEQ ID:4356.

[55672] Another function of VGAM1645 is therefore inhibition of LOC203292 (Accession XM\_117527). Accordingly, utilities of VGAM1645 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203292. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1646 (VGAM1646) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55673] VGAM1646 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1646 was detected is described hereinabove with reference to Figs. 1–8.

[55674] VGAM1646 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Dengue Virus. VGAM1646 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55675] VGAM1646 gene encodes a VGAM1646 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1646 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1646 precursor RNA is designated SEQ ID:1632, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1632 is located at position 9914 relative to the genome of Dengue Virus.

- [55676] VGAM1646 precursor RNA folds onto itself, forming VGAM1646 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [55677] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1646 folded precursor RNA into VGAM1646 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1646 RNA is designated SEQ ID:4357, and is provided hereinbelow with reference to the sequence listing part.

[55678] VGAM1646 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1646 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1646 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[55679] VGAM1646 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1646 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1646 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the



number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1646 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1646 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55680] The complementary binding of VGAM1646 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1646 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1646 host target RNA into VGAM1646 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55681] It is appreciated that VGAM1646 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1646 host target genes. The mRNA of each one of this plurality of VGAM1646 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1646 RNA, herein designated VGAM RNA, and which when bound by VGAM1646 RNA causes inhibition of translation of respective one or more VGAM1646 host target proteins.

[55682] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1646 gene, herein designated VGAM GENE, on one or more VGAM1646 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55683] It is yet further appreciated that a function of VGAM1646 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1646 include diagnosis, prevention and treatment of viral infection by Dengue Virus. Specific functions, and accordingly utilities, of VGAM1646 correlate with, and may be deduced from, the identity of the host target genes which VGAM1646 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55684] Nucleotide sequences of the VGAM1646 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1646 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1646 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1646 are further described hereinbelow with reference to Table 1.

[55685] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1646 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1646 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[55686] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1646 gene, herein designated VGAM is inhibition of expression of VGAM1646 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1646 correlate with, and may be deduced from, the identity of the target genes which VGAM1646 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55687] WW45 (Accession NM\_021818) is a VGAM1646 host target gene. WW45 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WW45, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WW45 BINDING SITE, designated SEQ ID:22396, to the nucleotide sequence of VGAM1646 RNA, herein designated VGAM RNA, also designated SEQ ID:4357.

[55688] A function of VGAM1646 is therefore inhibition of WW45 (Accession NM\_021818), a gene which is required for ubiquitination and therefore degradation of several cell surface proteins like gap1, fur4, mal61 and ste2. also acts

on rbp1. Accordingly, utilities of VGAM1646 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WW45. The function of WW45 has been established by previous studies. By searching an EST database using *C. elegans* and *Drosophila* WW domain-containing protein sequences as bait, followed by 5-prime and 3-prime RACE using a human heart cDNA library, Valverde (2000) obtained a full-length cDNA encoding WW45. The deduced 383-amino acid protein has a predicted molecular mass of approximately 45 kD. It contains 2 WW domains, a region rich in prolines and glutamines, and a coiled-coil region, as well as a nuclear localization signal and 2 endoplasmic reticulum retention signals. The mouse Ww45 cDNA has a different 3-prime untranslated region and encodes a protein that shares 93% identity with human WW45. Northern blot and RT-PCR analyses demonstrated that both human and mouse WW45 transcripts (1.2 and 2.7 kb, respectively) are ubiquitously expressed in adult tissues. In human, highest expression was in pancreas, while in mouse, highest expression was in testis. Northern blot analysis of whole mouse embryos showed that embryonic expression of Ww45 first occurred at 7 days postcoitum. Expression levels markedly

decreased at day 11 and remained low at days 15 and 17, suggesting that WW45 expression is developmentally regulated. Accordingly, expression of human WW45 was found to be higher in fetal heart than in adult heart. By radiation hybrid analysis, Valverde (2000) mapped the WW45 gene to chromosome 14q13–q23. In a screen for *Drosophila* mutations that result in tissue overgrowth, Tapon et al. (2002) identified salvador (sav), a gene that promotes both cell cycle exit and cell death. Elevated cyclin E (OMIM Ref. No. 123837) and inhibitor of apoptosis-1 (Diap1) levels were found in mutant cells, resulting in delayed cell cycle exit and impaired apoptosis. Salvador contains 2 WW domains and binds to the Warts (or OMIM Ref. No. 603473) protein kinase. Because WW45 is the human ortholog of salvador, Tapon et al. (2002) sequenced the entire WW45 coding region in a panel of 52 tumor-derived cell lines, representing a broad range of tissue types. One colon cancer cell line, HCT15, had a heterozygous C-to-A mutation at nucleotide 554, resulting in an asp185-to-ala substitution. This mutation was not present in 185 population-based controls (370 chromosomes), indicating that it is not a common polymorphism. The authors noted that HCT15 carries a mutation in the

mismatch repair gene MSH6 (OMIM Ref. No. 600678), which appears to enhance the frequency of point mutations in other genes. Two renal cancer cell lines, ACHN and 786-O, had deletions involving WW45. The normal allele was not present in either cell line, indicating that these cell lines were either homozygous or hemizygous for the deletion. The WW45 transcript was undetectable by RT-PCR in both cell lines, and a Southern blot using a probe derived from the 3-prime portion of the gene demonstrated that this part of the gene was absent in both cell lines. In cell line 786-O, PCR analysis of genomic DNA indicated that there was a deletion of approximately 157 kb, with the 5-prime breakpoint between exons 2 and 3 of WW45. The deletion in ACHN of approximately 138 kb encompassed the entire gene. The common region of overlap between these 2 deletions was only 21 kb, containing exons 3 to 5 of WW45. No other transcription units were identified within this 21 kb interval.

[55689] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55690] Tapon, N.; Harvey, K. F.; Bell, D. W.; Wahrer, D. C. R.; Schiripo, T. A.; Haber, D. A.; Hariharan, I. K. : salvador

promotes both cell cycle exit and apoptosis in *Drosophila* and is mutated in human cancer cell lines. *Cell* 110: 467–478, 2002. ; and

- [55691] Valverde, P. : Cloning, expression, and mapping of hWW45, a novel human WW domain-containing gene. *Biochem. Biophys. Res. Commun.* 276: 990–998, 2000.
- [55692] Further studies establishing the function and utilities of WW45 are found in John Hopkins OMIM database record ID 607203, and in cited publications numbered 5562–5563 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA1034 (Accession XM\_031223) is another VGAM1646 host target gene. KIAA1034 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1034 BINDING SITE, designated SEQ ID:31310, to the nucleotide sequence of VGAM1646 RNA, herein designated VGAM RNA, also designated SEQ ID:4357.
- [55693] Another function of VGAM1646 is therefore inhibition of KIAA1034 (Accession XM\_031223). Accordingly, utilities



of VGAM1646 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1034. SV2B (Accession NM\_014848) is another VGAM1646 host target gene. SV2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SV2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SV2B BINDING SITE, designated SEQ ID:16882, to the nucleotide sequence of VGAM1646 RNA, herein designated VGAM RNA, also designated SEQ ID:4357.

[55694] Another function of VGAM1646 is therefore inhibition of SV2B (Accession NM\_014848). Accordingly, utilities of VGAM1646 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SV2B. LOC219738 (Accession NM\_145306) is another VGAM1646 host target gene. LOC219738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC219738 BINDING SITE, designated SEQ ID:29818, to the nucleotide sequence of VGAM1646 RNA, herein designated VGAM RNA, also designated SEQ ID:4357.

[55695] Another function of VGAM1646 is therefore inhibition of LOC219738 (Accession NM\_145306). Accordingly, utilities of VGAM1646 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219738. LOC220573 (Accession XM\_045569) is another VGAM1646 host target gene. LOC220573 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220573 BINDING SITE, designated SEQ ID:34482, to the nucleotide sequence of VGAM1646 RNA, herein designated VGAM RNA, also designated SEQ ID:4357.

[55696] Another function of VGAM1646 is therefore inhibition of LOC220573 (Accession XM\_045569). Accordingly, utilities of VGAM1646 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220573. LOC91960 (Accession XM\_041872) is another VGAM1646 host target gene. LOC91960 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91960 BINDING SITE, designated SEQ ID:33611, to the nucleotide sequence of VGAM1646 RNA, herein designated VGAM RNA, also designated SEQ ID:4357.

[55697] Another function of VGAM1646 is therefore inhibition of LOC91960 (Accession XM\_041872). Accordingly, utilities of VGAM1646 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91960. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1647 (VGAM1647) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55698] VGAM1647 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1647 was detected is described hereinabove with reference to Figs. 1–8.

[55699] VGAM1647 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1647 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55700] VGAM1647 gene encodes a VGAM1647 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1647 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1647 precursor RNA is designated SEQ ID:1633, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1633 is located at position 104577 relative to the genome of Human Herpesvirus 8.

[55701] VGAM1647 precursor RNA folds onto itself, forming VGAM1647 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[55702] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1647 folded precursor RNA into VGAM1647 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1647 RNA is designated SEQ ID:4358, and is provided hereinbelow with reference to the sequence listing part.

[55703] VGAM1647 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1647 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1647 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55704] VGAM1647 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1647 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1647 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1647 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1647 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[55705] The complementary binding of VGAM1647 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1647 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1647 host target RNA into VGAM1647 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55706] It is appreciated that VGAM1647 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1647 host target genes. The mRNA of each one of this plurality of VGAM1647 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1647 RNA, herein designated VGAM RNA, and which when bound by VGAM1647 RNA causes inhibition of translation of respective one or more VGAM1647 host target proteins.

[55707] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1647 gene, herein designated VGAM GENE, on one or more VGAM1647 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55708] It is yet further appreciated that a function of VGAM1647 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1647 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1647 correlate with, and may be deduced from, the identity of the host target genes which VGAM1647 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55709] Nucleotide sequences of the VGAM1647 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1647 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1647 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, of VGAM1647 are further described hereinbelow with reference to Table 1.

[55710] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1647 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1647 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55711] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1647 gene, herein designated VGAM is inhibition of expression of VGAM1647 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1647 correlate with, and may be deduced from, the identity of the target genes which VGAM1647 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55712] Calpain 1, (mu/I) Large Subunit (CAPN1, Accession NM\_005186) is a VGAM1647 host target gene. CAPN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of CAPN1 BINDING SITE, designated SEQ ID:11686, to the nucleotide sequence of VGAM1647 RNA, herein designated VGAM RNA, also designated SEQ ID:4358.

[55713] A function of VGAM1647 is therefore inhibition of Calpain 1, ( $\mu$ /I) Large Subunit (CAPN1, Accession NM\_005186), a gene which is an intracellular protease that requires calcium for its catalytic activity. Accordingly, utilities of VGAM1647 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN1. The function of CAPN1 has been established by previous studies. Calpain (calcium-dependent protease; EC 3.4.22.17) is an intracellular protease that requires calcium for its catalytic activity. Two isozymes (CANP1 and CANP2), with different calcium requirements, have been identified. Both are heterodimers composed of L (large, catalytic, 80 kD) and S (small, regulatory, 30 kD) subunits. The isozymes share an identical S subunit (OMIM Ref. No. 114170); differences arise from the L subunits (L1 and L2). Using cDNA clones as probes, Ohno et al. (1989, 1990) mapped the CANPL1 and CANPL2 genes as well as the CANPS gene and a gene for another protein, L3, that is homologous to the other 2 L subunits; they used a combi-

nation of spot blot hybridization with sorted chromosomes and Southern hybridization with human-mouse cell hybrid DNAs. In this way they were able to assign CANPL1 to chromosome 11; CANPL2 to chromosome 1; CANPL3 to chromosome 15; and CANPS to chromosome 19.

Courseaux et al. (1996) used a combination of methods to refine maps of the approximately 5-Mb region of 11q13 that includes MEN1 (OMIM Ref. No. 131100). They proposed the following gene order: cen-

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PGA-

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FTH1--UGB--AHNAK--ROM1--MDU1--CHRM1--COX8--  
EMK1--FKBP2--PLCB3--[PYGM,  
ZFM1]--FAU--CAPN1--[MLK3,  
RELA]--FOSL1--SEA--CFL1--tel.

[55714] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55715] Ohno, S.; Minoshima, S.; Kudoh, J.; Fukuyama, R.; Shimizu, Y.; Ohmi-Imajoh, S.; Shimizu, N.; Suzuki, K. : Four genes for the calpain family locate on four distinct human chromosomes. Cytogenet. Cell Genet. 53: 225-229, 1990. ;

and

[55716] Courseaux, A.; Grosgeorge, J.; Gaudray, P.; Pannett, A. A. J.; Forbes, S. A.; Williamson, C.; Bassett, D.; Thakker, R. V.; Teh, B. T.; Farnebo, F.; Shepherd, J.; Skogseid, B.; Larsson, C.

[55717] Further studies establishing the function and utilities of CAPN1 are found in John Hopkins OMIM database record ID 114220, and in cited publications numbered 398 and 12571–12572 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0329 (Accession NM\_014844) is another VGAM1647 host target gene. KIAA0329 BINDING SITE1 and KIAA0329 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0329, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0329 BINDING SITE1 and KIAA0329 BINDING SITE2, designated SEQ ID:16873 and SEQ ID:16874 respectively, to the nucleotide sequence of VGAM1647 RNA, herein designated VGAM RNA, also designated SEQ ID:4358.

[55718] Another function of VGAM1647 is therefore inhibition of

KIAA0329 (Accession NM\_014844). Accordingly, utilities of VGAM1647 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0329. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1648 (VGAM1648) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55719] VGAM1648 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1648 was detected is described hereinabove with reference to Figs. 1-8.

[55720] VGAM1648 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1648 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55721] VGAM1648 gene encodes a VGAM1648 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1648 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1648 precursor RNA is designated SEQ ID:1634, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1634 is located at position 111049 relative to the genome of Human Herpesvirus 8.

- [55722] VGAM1648 precursor RNA folds onto itself, forming VGAM1648 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [55723] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1648 folded precursor RNA into VGAM1648 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide se-

quence of VGAM1648 RNA is designated SEQ ID:4359, and is provided hereinbelow with reference to the sequence listing part.

[55724] VGAM1648 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1648 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1648 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55725] VGAM1648 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1648 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1648 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1648 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1648 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[55726] The complementary binding of VGAM1648 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1648 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1648 host target RNA into VGAM1648 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55727] It is appreciated that VGAM1648 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1648 host target genes. The mRNA of each one of this plurality of VGAM1648 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1648 RNA, herein designated VGAM RNA, and which when bound by VGAM1648 RNA causes inhibition of translation of respective one or more VGAM1648 host target proteins.

[55728] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1648 gene, herein designated VGAM GENE, on one or more VGAM1648 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55729] It is yet further appreciated that a function of VGAM1648

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1648 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1648 correlate with, and may be deduced from, the identity of the host target genes which VGAM1648 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55730] Nucleotide sequences of the VGAM1648 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1648 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1648 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1648 are further described hereinbelow with reference to Table 1.

[55731] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1648 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1648 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55732] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1648 gene, herein designated VGAM is inhibition of expression of VGAM1648 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1648 correlate with, and may be deduced from, the identity of the target genes which VGAM1648 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55733] Lactate Dehydrogenase B (LDHB, Accession NM\_002300) is a VGAM1648 host target gene. LDHB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LDHB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDHB BINDING SITE, designated SEQ ID:8085, to the nucleotide sequence of VGAM1648 RNA, herein designated VGAM RNA, also designated SEQ ID:4359.

[55734] A function of VGAM1648 is therefore inhibition of Lactate Dehydrogenase B (LDHB, Accession NM\_002300), a gene which causes dehydrogenation of lactate. Accordingly, utilities of VGAM1648 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with LDHB. The function of LDHB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM273. Paired Box Gene 6 (aniridia, keratitis) (PAX6, Accession NM\_000280) is another VGAM1648 host target gene. PAX6 BINDING SITE1 and PAX6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PAX6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAX6 BINDING SITE1 and PAX6 BINDING SITE2, designated SEQ ID:5826 and SEQ ID:7310 respectively, to the nucleotide sequence of VGAM1648 RNA, herein designated VGAM RNA, also designated SEQ ID:4359.

[55735] Another function of VGAM1648 is therefore inhibition of Paired Box Gene 6 (aniridia, keratitis) (PAX6, Accession NM\_000280), a gene which involves in oculogenesis. Accordingly, utilities of VGAM1648 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAX6. The function of PAX6 and its association with various diseases and clinical conditions, has been established by previous studies, as described here-

in above with reference to VGAM1499.FLJ14594 (Accession NM\_032808) is another VGAM1648 host target gene. FLJ14594 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14594, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14594 BINDING SITE, designated SEQ ID:26567, to the nucleotide sequence of VGAM1648 RNA, herein designated VGAM RNA, also designated SEQ ID:4359.

[55736] Another function of VGAM1648 is therefore inhibition of FLJ14594 (Accession NM\_032808). Accordingly, utilities of VGAM1648 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14594. KIAA1908 (Accession XM\_055834) is another VGAM1648 host target gene. KIAA1908 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1908 BINDING SITE, designated SEQ ID:36331, to the

nucleotide sequence of VGAM1648 RNA, herein designated VGAM RNA, also designated SEQ ID:4359.

[55737] Another function of VGAM1648 is therefore inhibition of KIAA1908 (Accession XM\_055834). Accordingly, utilities of VGAM1648 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1908. MGC15875 (Accession NM\_032921) is another VGAM1648 host target gene. MGC15875 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15875, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15875 BINDING SITE, designated SEQ ID:26747, to the nucleotide sequence of VGAM1648 RNA, herein designated VGAM RNA, also designated SEQ ID:4359.

[55738] Another function of VGAM1648 is therefore inhibition of MGC15875 (Accession NM\_032921). Accordingly, utilities of VGAM1648 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15875. Ras and Rab Interactor 3 (RIN3, Accession NM\_024832) is another VGAM1648 host target gene. RIN3 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by RIN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RIN3 BINDING SITE, designated SEQ ID:24232, to the nucleotide sequence of VGAM1648 RNA, herein designated VGAM RNA, also designated SEQ ID:4359.

[55739] Another function of VGAM1648 is therefore inhibition of Ras and Rab Interactor 3 (RIN3, Accession NM\_024832). Accordingly, utilities of VGAM1648 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RIN3. UREB1 (Accession NM\_031407) is another VGAM1648 host target gene. UREB1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by UREB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UREB1 BINDING SITE, designated SEQ ID:25365, to the nucleotide sequence of VGAM1648 RNA, herein designated VGAM RNA, also designated SEQ ID:4359.

[55740] Another function of VGAM1648 is therefore inhibition of UREB1 (Accession NM\_031407). Accordingly, utilities of

VGAM1648 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UREB1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1649 (VGAM1649) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55741] VGAM1649 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1649 was detected is described hereinabove with reference to Figs. 1–8.

[55742] VGAM1649 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1649 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55743] VGAM1649 gene encodes a VGAM1649 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1649 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1649 precursor RNA is desig-



nated SEQ ID:1635, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1635 is located at position 105452 relative to the genome of Human Herpesvirus 8.

- [55744] VGAM1649 precursor RNA folds onto itself, forming VGAM1649 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [55745] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1649 folded precursor RNA into VGAM1649 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 60%) nucleotide sequence of VGAM1649 RNA is designated SEQ ID:4360, and is provided hereinbelow with reference to the sequence

listing part.

[55746] VGAM1649 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1649 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1649 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55747] VGAM1649 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1649 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1649 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1649 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1649 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55748] The complementary binding of VGAM1649 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1649 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1649 host target RNA into VGAM1649 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55749] It is appreciated that VGAM1649 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1649 host target genes. The mRNA of each one of this plurality of VGAM1649 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1649 RNA, herein designated VGAM

RNA, and which when bound by VGAM1649 RNA causes inhibition of translation of respective one or more VGAM1649 host target proteins.

[55750] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1649 gene, herein designated VGAM GENE, on one or more VGAM1649 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55751] It is yet further appreciated that a function of VGAM1649 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1649 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1649 correlate with, and may be deduced from, the identity of the host target genes which VGAM1649 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55752] Nucleotide sequences of the VGAM1649 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1649 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1649 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1649 are further described hereinbelow with reference to Table 1.

[55753] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1649 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1649 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55754] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1649 gene, herein designated VGAM is

inhibition of expression of VGAM1649 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1649 correlate with, and may be deduced from, the identity of the target genes which VGAM1649 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55755] Cholinergic Receptor, Nicotinic, Alpha Polypeptide 4 (CHRNA4, Accession NM\_000744) is a VGAM1649 host target gene. CHRNA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRNA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRNA4 BINDING SITE, designated SEQ ID:6397, to the nucleotide sequence of VGAM1649 RNA, herein designated VGAM RNA, also designated SEQ ID:4360.

[55756] A function of VGAM1649 is therefore inhibition of Cholinergic Receptor, Nicotinic, Alpha Polypeptide 4 (CHRNA4, Accession NM\_000744), a gene which binds acetylcholine and opens an ion-conducting channel across the plasma membrane. Accordingly, utilities of VGAM1649 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with CHRNA4. The function of CHRNA4 has been established by previous studies. Type 1 benign neonatal epilepsy (EBN1) was shown to be caused by mutations in the KCNQ2 gene (OMIM Ref. No. 602235) (Singh et al., 1998). The finding of a presumed mutation (Beck et al., 1994) in the CHRNA4 gene, which maps to the same region, in 1 of 20 families, was presumably an error. Steinlein et al. (1995) demonstrated a missense mutation in the CHRNA4 gene (118504.0002) associated with autosomal dominant nocturnal frontal lobe epilepsy (OMIM Ref. No. 600513), which had previously been mapped to 20q. Indeed, the mutation was sought because CHRNA4 maps to the same region of 20q and the gene is expressed in all layers of the frontal cortex. Mutations in the CHRNA4 gene appear to account for only a small proportion of the cases of nocturnal frontal lobe epilepsy. In a large Australian kindred, autosomal dominant nocturnal frontal lobe epilepsy was mapped to 20q13.2–q13.3 by Phillips et al. (1995). In affected members of the same family, Steinlein et al. (1995) used single-strand conformation analysis to detect an abnormality which by direct sequencing was demonstrated to be a C-to-T transition. It resulted in replacement of the neutral serine by the com-

plex aromatic phenylalanine (ser248-to-phe) in the sixth amino acid position of the transmembrane domain 2 (M2). They suggested that the mutation caused reduced receptor function. Forman et al. (1996) suggested an alternative mechanism for pathogenesis of epilepsy associated with this CHRNA4 mutation. From studies of the mouse muscle alpha-1 nicotinic receptor (OMIM Ref. No. 100690) noted in Forman et al. (1995), Forman et al. (1996) speculated that the mutation in CHRNA4 may cause receptor hyperactivity that could lead to epileptic activity. Animal model experiments lend further support to the function of CHRNA4. Marubio et al. (1999) disrupted the alpha-4 subunit of the neuronal nicotinic acetylcholine receptor by homologous recombination and studied homozygous alpha-4 null mice and mice lacking the beta-2 subunit of the nAChR. The homozygous alpha-4  $-/-$  mice no longer expressed high-affinity nicotine binding sites throughout the brain. In addition, both types of mutant mice displayed a reduced antinociceptive effect of nicotine on the hot-plate test and diminished sensitivity to nicotine in the tail-flick test. Patch-clamp recordings revealed that raphe magnus and thalamic neurons no longer responded to nicotine. Marubio et al. (1999) stated that the alpha-4



nAChR subunit, thought to associate with the beta-2 nAChR subunit, is therefore crucial for nicotine-elicited antinociception.

[55757] It is appreciated that the abovementioned animal model for CHRNA4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[55758] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55759] Steinlein, O. K.; Mulley, J. C.; Propping, P.; Wallace, R. H.; Phillips, H. A.; Sutherland, G. R.; Scheffer, I. E.; Berkovic, S. F. : A missense mutation in the neuronal nicotinic acetylcholine receptor alpha-4 subunit is associated with autosomal dominant nocturnal frontal lobe epilepsy. *Nature Genet.* 11: 201-203, 1995. ; and

[55760] Forman, S. A.; Yellen, G.; Thiele, E. A. : Alternative mechanism for pathogenesis of an inherited epilepsy by a nicotinic AChR mutation. (Letter) *Nature Genet.* 13: 396-397, 1996.

[55761] Further studies establishing the function and utilities of CHRNA4 are found in John Hopkins OMIM database record ID 118504, and in cited publications numbered 4452,

4662, 394–398, 7207–7208, 39 and 4663–403 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Coagulation Factor VII (serum prothrombin conversion accelerator) (F7, Accession NM\_000131) is another VGAM1649 host target gene. F7 BINDING SITE1 and F7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by F7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F7 BINDING SITE1 and F7 BINDING SITE2, designated SEQ ID:5605 and SEQ ID:21234 respectively, to the nucleotide sequence of VGAM1649 RNA, herein designated VGAM RNA, also designated SEQ ID:4360.

[55762] Another function of VGAM1649 is therefore inhibition of Coagulation Factor VII (serum prothrombin conversion accelerator) (F7, Accession NM\_000131). Accordingly, utilities of VGAM1649 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F7. KIAA0435 (Accession NM\_014801) is another VGAM1649 host target gene. KIAA0435 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0435 BINDING SITE, designated SEQ ID:16722, to the nucleotide sequence of VGAM1649 RNA, herein designated VGAM RNA, also designated SEQ ID:4360.

[55763] Another function of VGAM1649 is therefore inhibition of KIAA0435 (Accession NM\_014801). Accordingly, utilities of VGAM1649 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0435. LOC154214 (Accession XM\_087876) is another VGAM1649 host target gene. LOC154214 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154214, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154214 BINDING SITE, designated SEQ ID:39466, to the nucleotide sequence of VGAM1649 RNA, herein designated VGAM RNA, also designated SEQ ID:4360.

[55764] Another function of VGAM1649 is therefore inhibition of LOC154214 (Accession XM\_087876). Accordingly, utilities

of VGAM1649 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154214. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1650 (VGAM1650) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55765] VGAM1650 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1650 was detected is described hereinabove with reference to Figs. 1-8.

[55766] VGAM1650 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1650 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55767] VGAM1650 gene encodes a VGAM1650 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1650 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1650 precursor RNA is designated SEQ ID:1636, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1636 is located at position 109181 relative to the genome of Human Herpesvirus 8.

[55768] VGAM1650 precursor RNA folds onto itself, forming VGAM1650 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55769] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1650 folded precursor RNA into VGAM1650 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1650 RNA is designated SEQ ID:4361, and

is provided hereinbelow with reference to the sequence listing part.

[55770] VGAM1650 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1650 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1650 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[55771] VGAM1650 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1650 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1650 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1650 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1650 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55772] The complementary binding of VGAM1650 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1650 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1650 host target RNA into VGAM1650 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55773] It is appreciated that VGAM1650 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1650 host target genes. The mRNA of each one of this plurality of VGAM1650 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1650 RNA, herein designated VGAM RNA, and which when bound by VGAM1650 RNA causes inhibition of translation of respective one or more VGAM1650 host target proteins.

[55774] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1650 gene, herein designated VGAM GENE, on one or more VGAM1650 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55775] It is yet further appreciated that a function of VGAM1650 is inhibition of expression of host target genes, as part of



a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1650 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1650 correlate with, and may be deduced from, the identity of the host target genes which VGAM1650 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55776] Nucleotide sequences of the VGAM1650 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1650 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1650 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1650 are further described hereinbelow with reference to Table 1.

[55777] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1650 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1650 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55778] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1650 gene, herein designated VGAM is inhibition of expression of VGAM1650 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1650 correlate with, and may be deduced from, the identity of the target genes which VGAM1650 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55779] SNL (Accession NM\_003088) is a VGAM1650 host target gene. SNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNL BINDING SITE, designated SEQ ID:9058, to the nucleotide sequence of VGAM1650 RNA, herein designated VGAM RNA, also designated SEQ ID:4361.

[55780] A function of VGAM1650 is therefore inhibition of SNL (Accession NM\_003088), a gene which organizes filamentous actin into bundles with a minimum of 4.1:1 actin/fascin ratio. Accordingly, utilities of VGAM1650 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNL. The function of SNL and its association with various diseases and clinical con-

ditions, has been established by previous studies, as described hereinabove with reference to VGAM675.DKFZp761A132 (Accession NM\_032296) is another VGAM1650 host target gene. DKFZp761A132 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761A132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761A132 BINDING SITE, designated SEQ ID:26076, to the nucleotide sequence of VGAM1650 RNA, herein designated VGAM RNA, also designated SEQ ID:4361.

[55781] Another function of VGAM1650 is therefore inhibition of DKFZp761A132 (Accession NM\_032296). Accordingly, utilities of VGAM1650 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761A132. GMPPB (Accession XM\_171044) is another VGAM1650 host target gene. GMPPB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GMPPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of GMPPB BINDING SITE, designated SEQ ID:45814, to the nucleotide sequence of VGAM1650 RNA, herein designated VGAM RNA, also designated SEQ ID:4361.

[55782] Another function of VGAM1650 is therefore inhibition of GMPPB (Accession XM\_171044). Accordingly, utilities of VGAM1650 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMPPB. KIAA0125 (Accession XM\_018203) is another VGAM1650 host target gene. KIAA0125 BINDING SITE1 and KIAA0125 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0125, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0125 BINDING SITE1 and KIAA0125 BINDING SITE2, designated SEQ ID:30343 and SEQ ID:16689 respectively, to the nucleotide sequence of VGAM1650 RNA, herein designated VGAM RNA, also designated SEQ ID:4361.

[55783] Another function of VGAM1650 is therefore inhibition of KIAA0125 (Accession XM\_018203). Accordingly, utilities of VGAM1650 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0125. LOC143437 (Accession XM\_096426) is another VGAM1650 host target gene. LOC143437 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143437 BINDING SITE, designated SEQ ID:40358, to the nucleotide sequence of VGAM1650 RNA, herein designated VGAM RNA, also designated SEQ ID:4361.

[55784] Another function of VGAM1650 is therefore inhibition of LOC143437 (Accession XM\_096426). Accordingly, utilities of VGAM1650 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143437. LOC145989 (Accession XM\_004815) is another VGAM1650 host target gene. LOC145989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145989 BINDING SITE, designated SEQ ID:29949, to the nucleotide sequence of VGAM1650 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4361.

[55785] Another function of VGAM1650 is therefore inhibition of LOC145989 (Accession XM\_004815). Accordingly, utilities of VGAM1650 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145989. LOC253531 (Accession XM\_172868) is another VGAM1650 host target gene. LOC253531 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253531, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253531 BINDING SITE, designated SEQ ID:46145, to the nucleotide sequence of VGAM1650 RNA, herein designated VGAM RNA, also designated SEQ ID:4361.

[55786] Another function of VGAM1650 is therefore inhibition of LOC253531 (Accession XM\_172868). Accordingly, utilities of VGAM1650 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253531. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1651 (VGAM1651) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55787] VGAM1651 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1651 was detected is described hereinabove with reference to Figs. 1–8.

[55788] VGAM1651 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1651 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55789] VGAM1651 gene encodes a VGAM1651 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1651 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1651 precursor RNA is designated SEQ ID:1637, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1637 is located at position 106255 relative to the genome of Human Herpesvirus 8.

[55790] VGAM1651 precursor RNA folds onto itself, forming

VGAM1651 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55791] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1651 folded precursor RNA into VGAM1651 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 78%) nucleotide sequence of VGAM1651 RNA is designated SEQ ID:4362, and is provided hereinbelow with reference to the sequence listing part.

[55792] VGAM1651 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1651 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1651 host target RNA



comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55793] VGAM1651 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1651 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1651 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1651 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1651 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55794] The complementary binding of VGAM1651 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1651 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1651 host target RNA into VGAM1651 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55795] It is appreciated that VGAM1651 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1651 host target genes. The mRNA of each one of this plurality of VGAM1651 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1651 RNA, herein designated VGAM RNA, and which when bound by VGAM1651 RNA causes inhibition of translation of respective one or more VGAM1651 host target proteins.

[55796] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1651 gene, herein designated VGAM GENE, on one or more VGAM1651 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55797] It is yet further appreciated that a function of VGAM1651 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1651 correlate with, and may be deduced from, the identity of the host target genes which VGAM1651 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[55798] Nucleotide sequences of the VGAM1651 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1651 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1651 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1651 are further described hereinbelow with reference to Table 1.

[55799] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1651 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1651 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55800] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1651 gene, herein designated VGAM is inhibition of expression of VGAM1651 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1651 correlate with, and may be deduced from, the identity of the target genes which VGAM1651 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[55801] V-abl Abelson Murine Leukemia Viral Oncogene Homolog 1 (ABL1, Accession NM\_005157) is a VGAM1651 host target gene. ABL1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ABL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABL1 BINDING SITE, designated SEQ ID:11639, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55802] A function of VGAM1651 is therefore inhibition of V-abl Abelson Murine Leukemia Viral Oncogene Homolog 1 (ABL1, Accession NM\_005157). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABL1. Chromosome 1 Open Reading Frame 17 (C1orf17, Accession XM\_042965) is another VGAM1651 host target gene. C1orf17 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C1orf17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of C1orf17 BINDING SITE, designated SEQ ID:33854, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55803] Another function of VGAM1651 is therefore inhibition of Chromosome 1 Open Reading Frame 17 (C1orf17, Accession XM\_042965). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf17. Chromosome 1 Open Reading Frame 34 (C1orf34, Accession XM\_027172) is another VGAM1651 host target gene. C1orf34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf34 BINDING SITE, designated SEQ ID:30432, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55804] Another function of VGAM1651 is therefore inhibition of Chromosome 1 Open Reading Frame 34 (C1orf34, Accession XM\_027172). Accordingly, utilities of VGAM1651 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf34. Chondrolectin (CHODL, Accession NM\_024944) is another VGAM1651 host target gene. CHODL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHODL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHODL BINDING SITE, designated SEQ ID:24493, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55805] Another function of VGAM1651 is therefore inhibition of Chondrolectin (CHODL, Accession NM\_024944). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHODL. DJ465N24.2.1 (Accession NM\_020317) is another VGAM1651 host target gene. DJ465N24.2.1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DJ465N24.2.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of DJ465N24.2.1 BINDING SITE, designated SEQ ID:21580, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55806] Another function of VGAM1651 is therefore inhibition of DJ465N24.2.1 (Accession NM\_020317). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ465N24.2.1. DKFZp547I014 (Accession NM\_020217) is another VGAM1651 host target gene. DKFZp547I014 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp547I014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I014 BINDING SITE, designated SEQ ID:21469, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55807] Another function of VGAM1651 is therefore inhibition of DKFZp547I014 (Accession NM\_020217). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated



with DKFZp547I014. FLJ13052 (Accession NM\_023018) is another VGAM1651 host target gene. FLJ13052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13052 BINDING SITE, designated SEQ ID:23284, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55808] Another function of VGAM1651 is therefore inhibition of FLJ13052 (Accession NM\_023018). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13052. KIAA0350 (Accession XM\_028332) is another VGAM1651 host target gene. KIAA0350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0350 BINDING SITE, designated SEQ ID:30659, to the nucleotide sequence of VGAM1651 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4362.

[55809] Another function of VGAM1651 is therefore inhibition of KIAA0350 (Accession XM\_028332). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0350. KIAA0980 (Accession NM\_025176) is another VGAM1651 host target gene. KIAA0980 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0980, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0980 BINDING SITE, designated SEQ ID:24810, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55810] Another function of VGAM1651 is therefore inhibition of KIAA0980 (Accession NM\_025176). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0980. KIAA1529 (Accession XM\_047336) is another VGAM1651 host target gene. KIAA1529 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1529, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1529 BINDING SITE, designated SEQ ID:34949, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55811] Another function of VGAM1651 is therefore inhibition of KIAA1529 (Accession XM\_047336). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1529. KIAA1617 (Accession XM\_166140) is another VGAM1651 host target gene. KIAA1617 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1617 BINDING SITE, designated SEQ ID:43943, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55812] Another function of VGAM1651 is therefore inhibition of KIAA1617 (Accession XM\_166140). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1617. KIAA1729 (Accession XM\_114418) is another VGAM1651 host target gene. KIAA1729 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1729, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1729 BINDING SITE, designated SEQ ID:42952, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55813] Another function of VGAM1651 is therefore inhibition of KIAA1729 (Accession XM\_114418). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1729. V-maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog B (avian) (MAFB, Accession NM\_005461) is another VGAM1651 host target gene. MAFB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of MAFB BINDING SITE, designated SEQ ID:11944, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55814] Another function of VGAM1651 is therefore inhibition of V-maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog B (avian) (MAFB, Accession NM\_005461). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAFB. MGC13040 (Accession NM\_032930) is another VGAM1651 host target gene. MGC13040 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC13040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13040 BINDING SITE, designated SEQ ID:26754, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55815] Another function of VGAM1651 is therefore inhibition of MGC13040 (Accession NM\_032930). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13040. MIC2 Like 1 (MIC2L1, Accession NM\_031462)

is another VGAM1651 host target gene. MIC2L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIC2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIC2L1 BINDING SITE, designated SEQ ID:25487, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55816] Another function of VGAM1651 is therefore inhibition of MIC2 Like 1 (MIC2L1, Accession NM\_031462). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIC2L1. RAI (Accession NM\_006663) is another VGAM1651 host target gene. RAI BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI BINDING SITE, designated SEQ ID:13473, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55817] Another function of VGAM1651 is therefore inhibition of RAI (Accession NM\_006663). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI. LOC152059 (Accession XM\_087372) is another VGAM1651 host target gene. LOC152059 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152059, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152059 BINDING SITE, designated SEQ ID:39206, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55818] Another function of VGAM1651 is therefore inhibition of LOC152059 (Accession XM\_087372). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152059. LOC152404 (Accession XM\_087460) is another VGAM1651 host target gene. LOC152404 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152404, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152404 BINDING SITE, designated SEQ ID:39272, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55819] Another function of VGAM1651 is therefore inhibition of LOC152404 (Accession XM\_087460). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152404. LOC197414 (Accession XM\_113880) is another VGAM1651 host target gene. LOC197414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197414 BINDING SITE, designated SEQ ID:42516, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55820] Another function of VGAM1651 is therefore inhibition of LOC197414 (Accession XM\_113880). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC197414. LOC221463 (Accession XM\_166374) is another VGAM1651 host target gene. LOC221463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221463 BINDING SITE, designated SEQ ID:44197, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55821] Another function of VGAM1651 is therefore inhibition of LOC221463 (Accession XM\_166374). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221463. LOC256222 (Accession XM\_173177) is another VGAM1651 host target gene. LOC256222 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256222 BINDING SITE, designated SEQ ID:46426, to the nucleotide sequence of VGAM1651 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4362.

[55822] Another function of VGAM1651 is therefore inhibition of LOC256222 (Accession XM\_173177). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256222. LOC57109 (Accession NM\_020385) is another VGAM1651 host target gene. LOC57109 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC57109, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57109 BINDING SITE, designated SEQ ID:21654, to the nucleotide sequence of VGAM1651 RNA, herein designated VGAM RNA, also designated SEQ ID:4362.

[55823] Another function of VGAM1651 is therefore inhibition of LOC57109 (Accession NM\_020385). Accordingly, utilities of VGAM1651 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57109. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1652 (VGAM1652) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55824] VGAM1652 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1652 was detected is described hereinabove with reference to Figs. 1–8.

[55825] VGAM1652 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yellow Fever Virus. VGAM1652 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55826] VGAM1652 gene encodes a VGAM1652 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1652 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1652 precursor RNA is designated SEQ ID:1638, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1638 is located at position 10776 relative to the genome of Yellow Fever Virus.

[55827] VGAM1652 precursor RNA folds onto itself, forming

VGAM1652 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55828] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1652 folded precursor RNA into VGAM1652 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1652 RNA is designated SEQ ID:4363, and is provided hereinbelow with reference to the sequence listing part.

[55829] VGAM1652 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1652 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1652 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55830] VGAM1652 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1652 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1652 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1652 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1652 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55831] The complementary binding of VGAM1652 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1652 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1652 host target RNA into VGAM1652 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55832] It is appreciated that VGAM1652 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1652 host target genes. The mRNA of each one of this plurality of VGAM1652 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1652 RNA, herein designated VGAM RNA, and which when bound by VGAM1652 RNA causes inhibition of translation of respective one or more VGAM1652 host target proteins.

[55833] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1652 gene, herein designated VGAM GENE, on one or more VGAM1652 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55834] It is yet further appreciated that a function of VGAM1652 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of viral infection by Yellow Fever Virus. Specific functions, and accordingly utilities, of VGAM1652 correlate with, and may be deduced from, the identity of the host target genes which VGAM1652 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[55835] Nucleotide sequences of the VGAM1652 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1652 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1652 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1652 are further described hereinbelow with reference to Table 1.

[55836] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1652 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1652 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55837] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1652 gene, herein designated VGAM is inhibition of expression of VGAM1652 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1652 correlate with, and may be deduced from, the identity of the target genes which VGAM1652 binds and inhibits, and the function of these target genes,



as elaborated hereinbelow.

[55838] Aryl–hydrocarbon Receptor Nuclear Translocator 2 (ARNT2, Accession NM\_014862) is a VGAM1652 host target gene. ARNT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNT2 BINDING SITE, designated SEQ ID:16937, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55839] A function of VGAM1652 is therefore inhibition of Aryl–hydrocarbon Receptor Nuclear Translocator 2 (ARNT2, Accession NM\_014862), a gene which specifically recognizes the xenobiotic response element (xre). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNT2. The function of ARNT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM345.Cholinergic Receptor, Nicotinic, Alpha Polypeptide 4 (CHRNA4, Accession

NM\_000744) is another VGAM1652 host target gene.

CHRNA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRNA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRNA4 BINDING SITE, designated SEQ ID:6398, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55840] Another function of VGAM1652 is therefore inhibition of Cholinergic Receptor, Nicotinic, Alpha Polypeptide 4 (CHRNA4, Accession NM\_000744), a gene which binds acetylcholine and opens an ion-conducting channel across the plasma membrane. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRNA4. The function of CHRNA4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1649. DiGeorge Syndrome Critical Region Gene 2 (DGCR2, Accession NM\_005137) is another VGAM1652 host target gene. DGCR2 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by DGCR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGCR2 BINDING SITE, designated SEQ ID:11612, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55841] Another function of VGAM1652 is therefore inhibition of DiGeorge Syndrome Critical Region Gene 2 (DGCR2, Accession NM\_005137), a gene which could intervene in cell-cell or cell-matrix interactions. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGCR2. The function of DGCR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1485. Ectodermal Dysplasia 1, Anhidrotic (ED1, Accession NM\_001399) is another VGAM1652 host target gene. ED1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ED1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

**BINDING SITE III.** Table 2 illustrates the complementarity of the nucleotide sequences of ED1 BINDING SITE, designated SEQ ID:7100, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55842] Another function of VGAM1652 is therefore inhibition of Ectodermal Dysplasia 1, Anhidrotic (ED1, Accession NM\_001399). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ED1. Ephrin-B1 (EFNB1, Accession NM\_004429) is another VGAM1652 host target gene. EFNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNB1 BINDING SITE, designated SEQ ID:10709, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55843] Another function of VGAM1652 is therefore inhibition of Ephrin-B1 (EFNB1, Accession NM\_004429), a gene which is a transmembrane ligand of Eph-related receptor tyro-

sine kinases, has a role in cell adhesion. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFN1. The function of EFN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM390. Glucagon-like Peptide 1 Receptor (GLP1R, Accession NM\_002062) is another VGAM1652 host target gene. GLP1R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLP1R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLP1R BINDING SITE, designated SEQ ID:7825, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55844] Another function of VGAM1652 is therefore inhibition of Glucagon-like Peptide 1 Receptor (GLP1R, Accession NM\_002062), a gene which is mediated by g proteins which activate adenylyl cyclase. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLP1R.

The function of GLP1R has been established by previous studies. Glucagon-like peptide-1 (GLP1) is a hormone derived from the proglucagon molecule (OMIM Ref. No. 138030) and is secreted by intestinal L cells. It is the most potent stimulator of glucose-induced insulin secretion and also suppresses in vivo acid secretion by gastric glands. By transient expression of a rat pancreatic islet cDNA library in COS cells, Thorens (1992) isolated a cDNA for the GLP1 receptor (GLP1R). Transfected into COS cells, the receptor bound GLP1 with high affinity and was coupled to activation of adenylate cyclase. It did not bind peptides of related structure and similar function, such as glucagon (GCG; 138030), gastric inhibitory polypeptide (GIP; 137240), vasoactive intestinal peptide (VIP; 192320), or secretin (SCT; 182099). The receptor is 463 amino acids long and contains 7 transmembrane domains. Sequence homology was found only with the receptors for secretin (SCTR; 182098), calcitonin (CALCR; 114131), and parathyroid hormone (PTHr; 168468), which together form a newly characterized family of G-coupled receptors. Dillon et al. (1993) also cloned a cDNA corresponding to the GLP1R gene. By promoter analysis and electrophoretic mobility shift analysis, Wildhage et al. (1999) showed that

the GLP1R promoter binds both SP1 (OMIM Ref. No. 189906) and SP3 (OMIM Ref. No. 601804). They concluded that the basal activity of the GLP1R gene is mediated by 2 proximal SP1-binding sites and that a more distal site acts as a repressor.

[55845] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55846] Dillon, J. S.; Tanizawa, Y.; Wheeler, M. B.; Leng, X.-H.; Ligon, B. B.; Rabin, D. U.; Yoo-Warren, H.; Permutt, M. A.; Boyd, A. E., III : Cloning and functional expression of the human glucagon-like peptide-1 (GLP-1) receptor. *Endocrinology* 133: 1907-1910, 1993. ; and

[55847] Wildhage, I.; Trusheim, H.; Goke, B.; Lankat-Buttgereit, B. : Gene expression of the human glucagon-like peptide-1 receptor is regulated by Sp1 and Sp3. *Endocrinology* 140: 624-631, 1999.

[55848] Further studies establishing the function and utilities of GLP1R are found in John Hopkins OMIM database record ID 138032, and in cited publications numbered 3167-317 and 3356 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Inositol Hexaphosphate Kinase 1 (IHPK1, Accession XM\_171045) is

another VGAM1652 host target gene. IHPK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IHPK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IHPK1 BINDING SITE, designated SEQ ID:45822, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55849] Another function of VGAM1652 is therefore inhibition of Inositol Hexaphosphate Kinase 1 (IHPK1, Accession XM\_171045), a gene which is a messenger molecule that releases calcium from intracellular stores. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IHPK1. The function of IHPK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1061. Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM\_012275) is another VGAM1652 host target gene. IL1F5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IL1F5, corresponding to a HOST



TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1F5 BINDING SITE, designated SEQ ID:14597, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55850] Another function of VGAM1652 is therefore inhibition of Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM\_012275), a gene which is a novel interleukin-1 receptor antagonist gene. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F5. The function of IL1F5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM263. Jumping Translocation Breakpoint (JTB, Accession NM\_006694) is another VGAM1652 host target gene. JTB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by JTB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JTB BINDING SITE, designated SEQ ID:13514, to the nu-

cleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55851] Another function of VGAM1652 is therefore inhibition of Jumping Translocation Breakpoint (JTB, Accession NM\_006694). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JTB. Leukemia Inhibitory Factor (cholinergic differentiation factor) (LIF, Accession NM\_002309) is another VGAM1652 host target gene. LIF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIF BINDING SITE, designated SEQ ID:8096, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55852] Another function of VGAM1652 is therefore inhibition of Leukemia Inhibitory Factor (cholinergic differentiation factor) (LIF, Accession NM\_002309). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIF. Multiple Endocrine Neoplasia I (MEN1, Accession

XM\_167804) is another VGAM1652 host target gene.

MEN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MEN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEN1 BINDING SITE, designated SEQ ID:44841, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55853] Another function of VGAM1652 is therefore inhibition of Multiple Endocrine Neoplasia I (MEN1, Accession XM\_167804). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEN1. Male-specific Lethal 3-like 1 (Drosophila) (MSL3L1, Accession NM\_006800) is another VGAM1652 host target gene. MSL3L1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MSL3L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSL3L1 BINDING SITE, designated SEQ ID:13670, to the nucleotide sequence of VGAM1652 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4363.

[55854] Another function of VGAM1652 is therefore inhibition of Male-specific Lethal 3-like 1 (Drosophila) (MSL3L1, Accession NM\_006800). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSL3L1. Phosphoinositide-3-kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM\_002646) is another VGAM1652 host target gene. PIK3C2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3C2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3C2B BINDING SITE, designated SEQ ID:8506, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55855] Another function of VGAM1652 is therefore inhibition of Phosphoinositide-3-kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM\_002646). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3C2B. Phosphomannomutase 2 (PMM2, Accession

XM\_050755) is another VGAM1652 host target gene.

PMM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMM2 BINDING SITE, designated SEQ ID:35678, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55856] Another function of VGAM1652 is therefore inhibition of Phosphomannomutase 2 (PMM2, Accession XM\_050755). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMM2. Prokineticin 1 (PROK1, Accession NM\_032414) is another VGAM1652 host target gene. PROK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PROK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROK1 BINDING SITE, designated SEQ ID:26198, to the nucleotide sequence of VGAM1652 RNA,

herein designated VGAM RNA, also designated SEQ ID:4363.

[55857] Another function of VGAM1652 is therefore inhibition of Prokineticin 1 (PROK1, Accession NM\_032414), a gene which induces proliferation, migration and fenestration in capillary endothelial cells derived from endocrine glands. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROK1. The function of PROK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1000.SH3-domain Binding Protein 2 (SH3BP2, Accession NM\_003023) is another VGAM1652 host target gene. SH3BP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP2 BINDING SITE, designated SEQ ID:8945, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55858] Another function of VGAM1652 is therefore inhibition of SH3-domain Binding Protein 2 (SH3BP2, Accession NM\_003023). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BP2. Solute Carrier Family 22 (organic anion/cation transporter), Member 12 (SLC22A12, Accession NM\_144585) is another VGAM1652 host target gene. SLC22A12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC22A12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC22A12 BINDING SITE, designated SEQ ID:29404, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55859] Another function of VGAM1652 is therefore inhibition of Solute Carrier Family 22 (organic anion/cation transporter), Member 12 (SLC22A12, Accession NM\_144585), a gene which is a urate -anion exchanger regulating blood urate levels. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC22A12. The function of

SLC22A12 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1034. Secreted Protein, Acidic, Cysteine-rich (osteonectin) (SPARC, Accession NM\_003118) is another VGAM1652 host target gene. SPARC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPARC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPARC BINDING SITE, designated SEQ ID:9089, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55860] Another function of VGAM1652 is therefore inhibition of Secreted Protein, Acidic, Cysteine-rich (osteonectin) (SPARC, Accession NM\_003118), a gene which appears to regulate cell growth through interactions with the extracellular matrix and cytokines. binds calcium and copper, several types of collagen, albumin, thrombospondin, pdgf and cell membranes. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPARC. The func-



tion of SPARC has been established by previous studies. PARC is identical to osteonectin (from Latin verb nectere, to bind, bridge or link), a protein important to bone calcification which was identified by Termine et al. (1981). It is a 32,000–dalton, bone–specific phosphoprotein that binds selectively to hydroxyapatite and to collagen fibrils at distinct sites. Osteonectin accounts for the unique property of bone collagen to undergo calcification; type I collagen of bone is identical to that of skin and tendon. In bone, it is present in a concentration of 2.3 micrograms per 10 micrograms of protein. It is present also in dentin but absent from all other tissues. By comparison of protein sequences as well as investigation of the genes, Findlay et al. (1988) concluded that osteonectin is highly conserved between species. Naylor et al. (1989) demonstrated RFLPs of the ON gene which should be useful as markers on chromosome 5 and for investigating the possible role of osteonectin in bone diseases. SPARC, which can be selectively expressed by the endothelium in response to certain types of injury, induces rounding in adherent endothelial cells in vitro. From the results of studies on the influence of SPARC on endothelial permeability, Goldblum et al. (1994) concluded that SPARC regulates endothelial

barrier function through F-actin-dependent changes in cell shape, coincident with the appearance of intercellular gaps, that provide a paracellular pathway for extravasation of macromolecules. Animal model experiments lend further support to the function of SPARC. Gilmour et al. (1998) generated mice deficient for SPARC by targeted disruption. SPARC-deficient mice appeared normal and fertile until around 6 months of age, when they developed severe eye pathology characterized by cataract formation and rupture of the lens capsule. The first sign of lens pathology occurred in the equatorial bow region where vacuoles gradually formed within differentiating epithelial cells and fiber cells. The lens capsule, however, showed no qualitative changes in the major basal lamina proteins laminin, collagen IV, perlecan, or entactin.

[55861] It is appreciated that the abovementioned animal model for SPARC is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[55862] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[55863] Gilmour, D. T.; Lyon, G. J.; Carlton, M. B. L.; Sanes, J. R.;

Cunningham, J. M.; Anderson, J. R.; Hogan, B. L. M.; Evans, M. J.; Colledge, W. H. : Mice deficient for the secreted glycoprotein SPARC/osteonectin/BM40 develop normally but show severe age-onset cataract formation and disruption of the lens. EMBO J. 17: 1860–1870, 1998. ; and

[55864] Le Beau et al. (1993) mapped the SPARC gene to 5q31.3–q32. SGoldblum, S. E.; Ding, X.; Funk, S. E.; Sage, E. H. : SPARC (secreted protein acidic and rich in cysteine) regulates endotheli.

[55865] Further studies establishing the function and utilities of SPARC are found in John Hopkins OMIM database record ID 182120, and in cited publications numbered 10706–10707, 1059 and 11667–10606 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TH1-like (Drosophila) (TH1L, Accession NM\_016397) is another VGAM1652 host target gene. TH1L BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TH1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TH1L BINDING SITE, designated SEQ ID:18537, to the nucleotide sequence of VGAM1652 RNA, herein

designated VGAM RNA, also designated SEQ ID:4363.

[55866] Another function of VGAM1652 is therefore inhibition of TH1-like (Drosophila) (TH1L, Accession NM\_016397). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TH1L. Transient Receptor Potential Cation Channel, Subfamily C, Member 1 (TRPC1, Accession NM\_003304) is another VGAM1652 host target gene. TRPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC1 BINDING SITE, designated SEQ ID:9307, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55867] Another function of VGAM1652 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 1 (TRPC1, Accession NM\_003304), a gene which acts as a non-voltage-sensitive store-operated  $Ca^{2+}$  channel. Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC1. The function of TRPC1

and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.AF9Q34 (Accession NM\_032552) is another VGAM1652 host target gene. AF9Q34 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by AF9Q34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AF9Q34 BINDING SITE, designated SEQ ID:26275, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55868] Another function of VGAM1652 is therefore inhibition of AF9Q34 (Accession NM\_032552). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AF9Q34. Angiomotin Like 1 (AMOTL1, Accession XM\_057045) is another VGAM1652 host target gene. AMOTL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AMOTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of AMOTL1 BINDING SITE, designated SEQ ID:36464, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55869] Another function of VGAM1652 is therefore inhibition of Angiomotin Like 1 (AMOTL1, Accession XM\_057045). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOTL1. Aquaporin 9 (AQP9, Accession NM\_020980) is another VGAM1652 host target gene. AQP9 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by AQP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP9 BINDING SITE, designated SEQ ID:21970, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55870] Another function of VGAM1652 is therefore inhibition of Aquaporin 9 (AQP9, Accession NM\_020980). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with AQP9. ARNTL2 (Accession NM\_020183) is another VGAM1652 host target gene. ARNTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARNTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNTL2 BINDING SITE, designated SEQ ID:21416, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55871] Another function of VGAM1652 is therefore inhibition of ARNTL2 (Accession NM\_020183). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNTL2. Basic Leucine Zipper Nuclear Factor 1 (JEM-1) (BLZF1, Accession NM\_003666) is another VGAM1652 host target gene. BLZF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BLZF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLZF1 BINDING SITE, designated SEQ ID:9750, to the nucleotide sequence of

VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55872] Another function of VGAM1652 is therefore inhibition of Basic Leucine Zipper Nuclear Factor 1 (JEM-1) (BLZF1, Accession NM\_003666). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLZF1. Chromosome 20 Open Reading Frame 160 (C20orf160, Accession NM\_080625) is another VGAM1652 host target gene. C20orf160 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf160 BINDING SITE, designated SEQ ID:27933, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55873] Another function of VGAM1652 is therefore inhibition of Chromosome 20 Open Reading Frame 160 (C20orf160, Accession NM\_080625). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



C20orf160. DKFZP547E2110 (Accession XM\_165676) is another VGAM1652 host target gene. DKFZP547E2110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP547E2110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP547E2110 BINDING SITE, designated SEQ ID:43730, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55874] Another function of VGAM1652 is therefore inhibition of DKFZP547E2110 (Accession XM\_165676). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP547E2110. DKFZP586F1524 (Accession NM\_015584) is another VGAM1652 host target gene. DKFZP586F1524 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586F1524, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586F1524 BINDING SITE,

designated SEQ ID:17855, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55875] Another function of VGAM1652 is therefore inhibition of DKFZP586F1524 (Accession NM\_015584). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586F1524. Fatty Acid Desaturase 2 (FADS2, Accession NM\_004265) is another VGAM1652 host target gene. FADS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FADS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FADS2 BINDING SITE, designated SEQ ID:10467, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55876] Another function of VGAM1652 is therefore inhibition of Fatty Acid Desaturase 2 (FADS2, Accession NM\_004265). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FADS2. FLJ00024 (Accession

XM\_033361) is another VGAM1652 host target gene. FLJ00024 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00024 BINDING SITE, designated SEQ ID:31895, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55877] Another function of VGAM1652 is therefore inhibition of FLJ00024 (Accession XM\_033361). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00024. FLJ10201 (Accession NM\_018023) is another VGAM1652 host target gene. FLJ10201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10201 BINDING SITE, designated SEQ ID:19762, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM

RNA, also designated SEQ ID:4363.

[55878] Another function of VGAM1652 is therefore inhibition of FLJ10201 (Accession NM\_018023). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10201. FLJ10330 (Accession NM\_018061) is another VGAM1652 host target gene. FLJ10330 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10330, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10330 BINDING SITE, designated SEQ ID:19831, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55879] Another function of VGAM1652 is therefore inhibition of FLJ10330 (Accession NM\_018061). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10330. FLJ10604 (Accession NM\_018154) is another VGAM1652 host target gene. FLJ10604 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10604, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10604 BINDING SITE, designated SEQ ID:19963, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55880] Another function of VGAM1652 is therefore inhibition of FLJ10604 (Accession NM\_018154). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10604. FLJ13181 (Accession NM\_025188) is another VGAM1652 host target gene. FLJ13181 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13181 BINDING SITE, designated SEQ ID:24827, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55881] Another function of VGAM1652 is therefore inhibition of FLJ13181 (Accession NM\_025188). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ13181. FLJ14050 (Accession XM\_016361) is another VGAM1652 host target gene. FLJ14050 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14050, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14050 BINDING SITE, designated SEQ ID:30255, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55882] Another function of VGAM1652 is therefore inhibition of FLJ14050 (Accession XM\_016361). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14050. FLJ14084 (Accession NM\_021637) is another VGAM1652 host target gene. FLJ14084 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14084 BINDING SITE, designated SEQ ID:22283, to the nucleotide

sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55883] Another function of VGAM1652 is therefore inhibition of FLJ14084 (Accession NM\_021637). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14084. FLJ14346 (Accession NM\_025029) is another VGAM1652 host target gene. FLJ14346 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14346 BINDING SITE, designated SEQ ID:24621, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55884] Another function of VGAM1652 is therefore inhibition of FLJ14346 (Accession NM\_025029). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14346. FLJ14816 (Accession NM\_032845) is another VGAM1652 host target gene. FLJ14816 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ14816, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14816 BINDING SITE, designated SEQ ID:26640, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55885] Another function of VGAM1652 is therefore inhibition of FLJ14816 (Accession NM\_032845). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14816. FLJ20297 (Accession NM\_017951) is another VGAM1652 host target gene. FLJ20297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20297 BINDING SITE, designated SEQ ID:19650, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55886] Another function of VGAM1652 is therefore inhibition of FLJ20297 (Accession NM\_017951). Accordingly, utilities of



VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20297. FLJ21313 (Accession NM\_023927) is another VGAM1652 host target gene. FLJ21313 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21313 BINDING SITE, designated SEQ ID:23409, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55887] Another function of VGAM1652 is therefore inhibition of FLJ21313 (Accession NM\_023927). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21313. GOLGIN-67 (Accession XM\_170772) is another VGAM1652 host target gene. GOLGIN-67 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GOLGIN-67, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGIN-

67 BINDING SITE, designated SEQ ID:45535, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55888] Another function of VGAM1652 is therefore inhibition of GOLGIN-67 (Accession XM\_170772). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGIN-67. KIAA0229 (Accession XM\_166478) is another VGAM1652 host target gene. KIAA0229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0229 BINDING SITE, designated SEQ ID:44400, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55889] Another function of VGAM1652 is therefore inhibition of KIAA0229 (Accession XM\_166478). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0229. KIAA0247 (Accession NM\_014734) is another VGAM1652 host target gene. KIAA0247 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0247 BINDING SITE, designated SEQ ID:16376, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55890] Another function of VGAM1652 is therefore inhibition of KIAA0247 (Accession NM\_014734). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0247. KIAA0275 (Accession NM\_014767) is another VGAM1652 host target gene. KIAA0275 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0275 BINDING SITE, designated SEQ ID:16550, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55891] Another function of VGAM1652 is therefore inhibition of

KIAA0275 (Accession NM\_014767). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0275. KIAA0596 (Accession XM\_031706) is another VGAM1652 host target gene. KIAA0596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0596 BINDING SITE, designated SEQ ID:31467, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55892] Another function of VGAM1652 is therefore inhibition of KIAA0596 (Accession XM\_031706). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0596. KIAA0682 (Accession NM\_016196) is another VGAM1652 host target gene. KIAA0682 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0682 BINDING SITE, designated SEQ ID:18290, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55893] Another function of VGAM1652 is therefore inhibition of KIAA0682 (Accession NM\_016196). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0682. KIAA0855 (Accession NM\_015003) is another VGAM1652 host target gene. KIAA0855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0855 BINDING SITE, designated SEQ ID:17374, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55894] Another function of VGAM1652 is therefore inhibition of KIAA0855 (Accession NM\_015003). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0855. KIAA0977 (Accession NM\_014900) is another

VGAM1652 host target gene. KIAA0977 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0977 BINDING SITE, designated SEQ ID:17082, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55895] Another function of VGAM1652 is therefore inhibition of KIAA0977 (Accession NM\_014900). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0977. KIAA1014 (Accession XM\_037205) is another VGAM1652 host target gene. KIAA1014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1014 BINDING SITE, designated SEQ ID:32570, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55896] Another function of VGAM1652 is therefore inhibition of KIAA1014 (Accession XM\_037205). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1014. KIAA1322 (Accession XM\_052626) is another VGAM1652 host target gene. KIAA1322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1322 BINDING SITE, designated SEQ ID:36030, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55897] Another function of VGAM1652 is therefore inhibition of KIAA1322 (Accession XM\_052626). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1322. KIAA1462 (Accession XM\_166132) is another VGAM1652 host target gene. KIAA1462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1462, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1462 BINDING SITE, designated SEQ ID:43924, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55898] Another function of VGAM1652 is therefore inhibition of KIAA1462 (Accession XM\_166132). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1462. KIAA1497 (Accession XM\_041431) is another VGAM1652 host target gene. KIAA1497 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1497 BINDING SITE, designated SEQ ID:33529, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55899] Another function of VGAM1652 is therefore inhibition of KIAA1497 (Accession XM\_041431). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



KIAA1497. KIAA1553 (Accession XM\_166320) is another VGAM1652 host target gene. KIAA1553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1553, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1553 BINDING SITE, designated SEQ ID:44143, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55900] Another function of VGAM1652 is therefore inhibition of KIAA1553 (Accession XM\_166320). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1553. KIAA1940 (Accession XM\_086981) is another VGAM1652 host target gene. KIAA1940 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1940 BINDING SITE, designated SEQ ID:39010, to the nucleotide sequence of VGAM1652 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4363.

[55901] Another function of VGAM1652 is therefore inhibition of KIAA1940 (Accession XM\_086981). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1940. Kinesin Family Member 13B (KIF13B, Accession NM\_015254) is another VGAM1652 host target gene. KIF13B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF13B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF13B BINDING SITE, designated SEQ ID:17582, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55902] Another function of VGAM1652 is therefore inhibition of Kinesin Family Member 13B (KIF13B, Accession NM\_015254). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF13B. MGC13061 (Accession NM\_032322) is another VGAM1652 host target gene. MGC13061 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by MGC13061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13061 BINDING SITE, designated SEQ ID:26127, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55903] Another function of VGAM1652 is therefore inhibition of MGC13061 (Accession NM\_032322). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13061. Neurogenic Differentiation 6 (NEUROD6, Accession NM\_022728) is another VGAM1652 host target gene. NEUROD6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NEUROD6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEUROD6 BINDING SITE, designated SEQ ID:22929, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55904] Another function of VGAM1652 is therefore inhibition of Neurogenic Differentiation 6 (NEUROD6, Accession NM\_022728). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEUROD6. NYD-SP29 (Accession XM\_059085) is another VGAM1652 host target gene. NYD-SP29 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NYD-SP29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NYD-SP29 BINDING SITE, designated SEQ ID:36862, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55905] Another function of VGAM1652 is therefore inhibition of NYD-SP29 (Accession XM\_059085). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NYD-SP29. p25 (Accession NM\_007030) is another VGAM1652 host target gene. p25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by p25, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of p25 BINDING SITE, designated SEQ ID:13895, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55906] Another function of VGAM1652 is therefore inhibition of p25 (Accession NM\_007030). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with p25. Parvin, Alpha (PARVA, Accession NM\_018222) is another VGAM1652 host target gene. PARVA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PARVA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PARVA BINDING SITE, designated SEQ ID:20146, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55907] Another function of VGAM1652 is therefore inhibition of Parvin, Alpha (PARVA, Accession NM\_018222). Accordingly, utilities of VGAM1652 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with PARVA. RAS Protein Activator Like 2 (RASAL2, Accession NM\_004841) is another VGAM1652 host target gene. RASAL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RASAL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASAL2 BINDING SITE, designated SEQ ID:11249, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55908] Another function of VGAM1652 is therefore inhibition of RAS Protein Activator Like 2 (RASAL2, Accession NM\_004841). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASAL2. Ring Finger Protein 38 (RNF38, Accession NM\_022781) is another VGAM1652 host target gene. RNF38 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RNF38, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of RNF38 BINDING SITE, designated SEQ ID:23060, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55909] Another function of VGAM1652 is therefore inhibition of Ring Finger Protein 38 (RNF38, Accession NM\_022781). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF38. Ring Finger Protein (C3HC4 type) 8 (RNF8, Accession NM\_003958) is another VGAM1652 host target gene. RNF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF8 BINDING SITE, designated SEQ ID:10101, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55910] Another function of VGAM1652 is therefore inhibition of Ring Finger Protein (C3HC4 type) 8 (RNF8, Accession NM\_003958). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with RNF8. RNA-binding Region (RNP1, RRM) Containing 2 (RNPC2, Accession NM\_004902) is another VGAM1652 host target gene. RNPC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNPC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNPC2 BINDING SITE, designated SEQ ID:11336, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55911] Another function of VGAM1652 is therefore inhibition of RNA-binding Region (RNP1, RRM) Containing 2 (RNPC2, Accession NM\_004902). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNPC2. SARM (Accession NM\_015077) is another VGAM1652 host target gene. SARM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SARM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SARM BINDING SITE, designated SEQ



ID:17460, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55912] Another function of VGAM1652 is therefore inhibition of SARM (Accession NM\_015077). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SARM. SEC10-like 1 (*S. cerevisiae*) (SEC10L1, Accession NM\_006544) is another VGAM1652 host target gene. SEC10L1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEC10L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC10L1 BINDING SITE, designated SEQ ID:13298, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55913] Another function of VGAM1652 is therefore inhibition of SEC10-like 1 (*S. cerevisiae*) (SEC10L1, Accession NM\_006544). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC10L1. SWI/SNF Related,

Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM\_006015) is another VGAM1652 host target gene. SMARCF1 BINDING SITE1 through SMARCF1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMARCF1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCF1 BINDING SITE1 through SMARCF1 BINDING SITE3, designated SEQ ID:12626, SEQ ID:20521 and SEQ ID:29164 respectively, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55914] Another function of VGAM1652 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM\_006015). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCF1. T-box 4 (TBX4, Accession NM\_018488) is another VGAM1652 host target gene. TBX4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by TBX4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBX4 BINDING SITE, designated SEQ ID:20545, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55915] Another function of VGAM1652 is therefore inhibition of T-box 4 (TBX4, Accession NM\_018488). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBX4. ZFP106 (Accession NM\_022473) is another VGAM1652 host target gene. ZFP106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP106 BINDING SITE, designated SEQ ID:22831, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55916] Another function of VGAM1652 is therefore inhibition of ZFP106 (Accession NM\_022473). Accordingly, utilities of

VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP106. LOC112868 (Accession XM\_053402) is another VGAM1652 host target gene. LOC112868 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC112868, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112868 BINDING SITE, designated SEQ ID:36082, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55917] Another function of VGAM1652 is therefore inhibition of LOC112868 (Accession XM\_053402). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112868. LOC124842 (Accession XM\_064333) is another VGAM1652 host target gene. LOC124842 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC124842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC124842 BINDING SITE, designated SEQ ID:37263, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55918] Another function of VGAM1652 is therefore inhibition of LOC124842 (Accession XM\_064333). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124842. LOC126302 (Accession XM\_059020) is another VGAM1652 host target gene. LOC126302 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126302 BINDING SITE, designated SEQ ID:36823, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55919] Another function of VGAM1652 is therefore inhibition of LOC126302 (Accession XM\_059020). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126302. LOC126661 (Accession XM\_059061) is another VGAM1652 host target gene. LOC126661 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC126661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126661 BINDING SITE, designated SEQ ID:36854, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55920] Another function of VGAM1652 is therefore inhibition of LOC126661 (Accession XM\_059061). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126661. LOC130355 (Accession XM\_059423) is another VGAM1652 host target gene. LOC130355 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC130355, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130355 BINDING SITE, designated SEQ ID:36989, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55921] Another function of VGAM1652 is therefore inhibition of

LOC130355 (Accession XM\_059423). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130355. LOC130752 (Accession XM\_059468) is another VGAM1652 host target gene. LOC130752 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130752, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130752 BINDING SITE, designated SEQ ID:37006, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55922] Another function of VGAM1652 is therefore inhibition of LOC130752 (Accession XM\_059468). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130752. LOC144501 (Accession XM\_096612) is another VGAM1652 host target gene. LOC144501 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC144501 BINDING SITE, designated SEQ ID:40423, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55923] Another function of VGAM1652 is therefore inhibition of LOC144501 (Accession XM\_096612). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144501. LOC145988 (Accession XM\_085290) is another VGAM1652 host target gene. LOC145988 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145988 BINDING SITE, designated SEQ ID:38039, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55924] Another function of VGAM1652 is therefore inhibition of LOC145988 (Accession XM\_085290). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145988. LOC149603 (Accession XM\_047499) is an-



other VGAM1652 host target gene. LOC149603 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149603, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149603 BINDING SITE, designated SEQ ID:34970, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55925] Another function of VGAM1652 is therefore inhibition of LOC149603 (Accession XM\_047499). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149603. LOC149619 (Accession XM\_097690) is another VGAM1652 host target gene. LOC149619 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149619 BINDING SITE, designated SEQ ID:41028, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55926] Another function of VGAM1652 is therefore inhibition of LOC149619 (Accession XM\_097690). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149619. LOC150819 (Accession XM\_097954) is another VGAM1652 host target gene. LOC150819 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150819, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150819 BINDING SITE, designated SEQ ID:41247, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55927] Another function of VGAM1652 is therefore inhibition of LOC150819 (Accession XM\_097954). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150819. LOC151521 (Accession XM\_098076) is another VGAM1652 host target gene. LOC151521 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151521, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151521 BINDING SITE, designated SEQ ID:41369, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55928] Another function of VGAM1652 is therefore inhibition of LOC151521 (Accession XM\_098076). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151521. LOC152765 (Accession XM\_087519) is another VGAM1652 host target gene. LOC152765 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152765, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152765 BINDING SITE, designated SEQ ID:39316, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55929] Another function of VGAM1652 is therefore inhibition of LOC152765 (Accession XM\_087519). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC152765. LOC152925 (Accession XM\_087559) is another VGAM1652 host target gene. LOC152925 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152925 BINDING SITE, designated SEQ ID:39332, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55930] Another function of VGAM1652 is therefore inhibition of LOC152925 (Accession XM\_087559). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152925. LOC204301 (Accession XM\_115306) is another VGAM1652 host target gene. LOC204301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204301 BINDING SITE, designated SEQ ID:43093, to the nucleotide sequence of VGAM1652 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4363.

[55931] Another function of VGAM1652 is therefore inhibition of LOC204301 (Accession XM\_115306). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204301. LOC205313 (Accession XM\_119628) is another VGAM1652 host target gene. LOC205313 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC205313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205313 BINDING SITE, designated SEQ ID:43594, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55932] Another function of VGAM1652 is therefore inhibition of LOC205313 (Accession XM\_119628). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205313. LOC221751 (Accession XM\_166370) is another VGAM1652 host target gene. LOC221751 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221751, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221751 BINDING SITE, designated SEQ ID:44192, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55933] Another function of VGAM1652 is therefore inhibition of LOC221751 (Accession XM\_166370). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221751. LOC253350 (Accession XM\_174261) is another VGAM1652 host target gene. LOC253350 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253350 BINDING SITE, designated SEQ ID:46587, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55934] Another function of VGAM1652 is therefore inhibition of LOC253350 (Accession XM\_174261). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC253350. LOC253981 (Accession XM\_171064) is another VGAM1652 host target gene. LOC253981 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253981 BINDING SITE, designated SEQ ID:45863, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55935] Another function of VGAM1652 is therefore inhibition of LOC253981 (Accession XM\_171064). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253981. LOC254358 (Accession XM\_170771) is another VGAM1652 host target gene. LOC254358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254358 BINDING SITE, designated SEQ ID:45531, to

the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55936] Another function of VGAM1652 is therefore inhibition of LOC254358 (Accession XM\_170771). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254358. LOC257476 (Accession XM\_028610) is another VGAM1652 host target gene. LOC257476 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257476 BINDING SITE, designated SEQ ID:30714, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55937] Another function of VGAM1652 is therefore inhibition of LOC257476 (Accession XM\_028610). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257476. LOC64102 (Accession NM\_022144) is another VGAM1652 host target gene. LOC64102 BINDING SITE is HOST TARGET binding site found in the 5' un-



translated region of mRNA encoded by LOC64102, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC64102 BINDING SITE, designated SEQ ID:22708, to the nucleotide sequence of VGAM1652 RNA, herein designated VGAM RNA, also designated SEQ ID:4363.

[55938] Another function of VGAM1652 is therefore inhibition of LOC64102 (Accession NM\_022144). Accordingly, utilities of VGAM1652 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC64102. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1653 (VGAM1653) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55939] VGAM1653 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1653 was detected is described hereinabove with reference to Figs. 1-8.

[55940] VGAM1653 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Yellow Fever Virus.

VGAM1653 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55941] VGAM1653 gene encodes a VGAM1653 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1653 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1653 precursor RNA is designated SEQ ID:1639, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1639 is located at position 2036 relative to the genome of Yellow Fever Virus.

[55942] VGAM1653 precursor RNA folds onto itself, forming VGAM1653 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[55943] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1653 folded precursor RNA into VGAM1653 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1653 RNA is designated SEQ ID:4364, and is provided hereinbelow with reference to the sequence listing part.

[55944] VGAM1653 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1653 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1653 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55945] VGAM1653 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1653 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1653 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1653 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1653 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55946] The complementary binding of VGAM1653 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1653 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1653

host target RNA into VGAM1653 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55947] It is appreciated that VGAM1653 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1653 host target genes. The mRNA of each one of this plurality of VGAM1653 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1653 RNA, herein designated VGAM RNA, and which when bound by VGAM1653 RNA causes inhibition of translation of respective one or more VGAM1653 host target proteins.

[55948] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1653 gene, herein designated VGAM GENE, on one or more VGAM1653 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55949] It is yet further appreciated that a function of VGAM1653 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1653 include diagnosis, prevention and treatment of viral infection by Yellow Fever Virus. Specific functions, and accordingly utilities, of VGAM1653 correlate with, and may be deduced from, the identity of the host target genes which VGAM1653 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55950] Nucleotide sequences of the VGAM1653 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1653 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1653 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1653 are further

described hereinbelow with reference to Table 1.

[55951] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1653 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1653 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55952] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1653 gene, herein designated VGAM is inhibition of expression of VGAM1653 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1653 correlate with, and may be deduced from, the identity of the target genes which VGAM1653 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55953] Inositol Hexaphosphate Kinase 3 (IHPK3, Accession NM\_054111) is a VGAM1653 host target gene. IHPK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IHPK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

IHPK3 BINDING SITE, designated SEQ ID:27653, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55954] A function of VGAM1653 is therefore inhibition of Inositol Hexaphosphate Kinase 3 (IHPK3, Accession NM\_054111). Accordingly, utilities of VGAM1653 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IHPK3. Retinal Degeneration, Slow (retinitis pigmentosa 7) (RDS, Accession NM\_000322) is another VGAM1653 host target gene. RDS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RDS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDS BINDING SITE, designated SEQ ID:5862, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55955] Another function of VGAM1653 is therefore inhibition of Retinal Degeneration, Slow (retinitis pigmentosa 7) (RDS, Accession NM\_000322), a gene which may function as an adhesion molecule involved in stabilization and compaction of outer segment disks or in the maintenance of



the curvature of the rim. Accordingly, utilities of VGAM1653 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDS. The function of RDS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM341. Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM\_003349) is another VGAM1653 host target gene. UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UBE2V1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3, designated SEQ ID:9369, SEQ ID:22521 and SEQ ID:22768 respectively, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55956] Another function of VGAM1653 is therefore inhibition of Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM\_003349), a gene which may play a role in signaling for DNA repair. Accordingly, utilities of VGAM1653

include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2V1. The function of UBE2V1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM155.FLJ12903 (Accession NM\_022753) is another VGAM1653 host target gene. FLJ12903 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12903, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12903 BINDING SITE, designated SEQ ID:22977, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55957] Another function of VGAM1653 is therefore inhibition of FLJ12903 (Accession NM\_022753). Accordingly, utilities of VGAM1653 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12903. KIAA0285 (Accession NM\_014807) is another VGAM1653 host target gene. KIAA0285 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0285, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0285 BINDING SITE, designated SEQ ID:16750, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55958] Another function of VGAM1653 is therefore inhibition of KIAA0285 (Accession NM\_014807). Accordingly, utilities of VGAM1653 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0285. KIAA0446 (Accession XM\_044155) is another VGAM1653 host target gene. KIAA0446 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0446, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0446 BINDING SITE, designated SEQ ID:34149, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55959] Another function of VGAM1653 is therefore inhibition of KIAA0446 (Accession XM\_044155). Accordingly, utilities of VGAM1653 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0446. KIAA0630 (Accession XM\_114729) is another VGAM1653 host target gene. KIAA0630 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0630 BINDING SITE, designated SEQ ID:43061, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55960] Another function of VGAM1653 is therefore inhibition of KIAA0630 (Accession XM\_114729). Accordingly, utilities of VGAM1653 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0630. KIAA0945 (Accession NM\_014952) is another VGAM1653 host target gene. KIAA0945 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0945 BINDING SITE, designated SEQ ID:17291, to the

nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55961] Another function of VGAM1653 is therefore inhibition of KIAA0945 (Accession NM\_014952). Accordingly, utilities of VGAM1653 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0945. SUN1 (Accession NM\_025154) is another VGAM1653 host target gene. SUN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SUN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUN1 BINDING SITE, designated SEQ ID:24793, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55962] Another function of VGAM1653 is therefore inhibition of SUN1 (Accession NM\_025154). Accordingly, utilities of VGAM1653 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUN1. LOC154881 (Accession XM\_088063) is another VGAM1653 host target gene. LOC154881 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC154881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154881 BINDING SITE, designated SEQ ID:39494, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55963] Another function of VGAM1653 is therefore inhibition of LOC154881 (Accession XM\_088063). Accordingly, utilities of VGAM1653 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154881. LOC254122 (Accession XM\_170660) is another VGAM1653 host target gene. LOC254122 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254122 BINDING SITE, designated SEQ ID:45435, to the nucleotide sequence of VGAM1653 RNA, herein designated VGAM RNA, also designated SEQ ID:4364.

[55964] Another function of VGAM1653 is therefore inhibition of LOC254122 (Accession XM\_170660). Accordingly, utilities

of VGAM1653 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254122. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1654 (VGAM1654) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55965] VGAM1654 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1654 was detected is described hereinabove with reference to Figs. 1-8.

[55966] VGAM1654 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yellow Fever Virus. VGAM1654 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55967] VGAM1654 gene encodes a VGAM1654 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1654 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1654 precursor RNA is designated SEQ ID:1640, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1640 is located at position 6577 relative to the genome of Yellow Fever Virus.

- [55968] VGAM1654 precursor RNA folds onto itself, forming VGAM1654 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [55969] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1654 folded precursor RNA into VGAM1654 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1654 RNA is designated SEQ ID:4365, and



is provided hereinbelow with reference to the sequence listing part.

[55970] VGAM1654 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1654 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1654 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[55971] VGAM1654 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1654 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1654 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1654 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1654 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[55972] The complementary binding of VGAM1654 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1654 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1654 host target RNA into VGAM1654 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55973] It is appreciated that VGAM1654 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1654 host target genes. The mRNA of each one of this plurality of VGAM1654 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1654 RNA, herein designated VGAM RNA, and which when bound by VGAM1654 RNA causes inhibition of translation of respective one or more VGAM1654 host target proteins.

[55974] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1654 gene, herein designated VGAM GENE, on one or more VGAM1654 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55975] It is yet further appreciated that a function of VGAM1654 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1654 include diagnosis, prevention and treatment of viral infection by Yellow Fever Virus. Specific functions, and accordingly utilities, of VGAM1654 correlate with, and may be deduced from, the identity of the host target genes which VGAM1654 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55976] Nucleotide sequences of the VGAM1654 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1654 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1654 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1654 are further described hereinbelow with reference to Table 1.

[55977] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1654 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1654 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55978] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1654 gene, herein designated VGAM is inhibition of expression of VGAM1654 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1654 correlate with, and may be deduced from, the identity of the target genes which VGAM1654 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[55979] Desmocollin 2 (DSC2, Accession NM\_004949) is a VGAM1654 host target gene. DSC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DSC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSC2 BINDING SITE, designated SEQ ID:11393, to the nucleotide sequence of VGAM1654 RNA, herein designated VGAM RNA, also designated SEQ ID:4365.

[55980] A function of VGAM1654 is therefore inhibition of Desmocollin 2 (DSC2, Accession NM\_004949), a gene which is a component of intercellular desmosome junctions. Accordingly, utilities of VGAM1654 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSC2. The function of DSC2 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM909. Ring Finger Protein 14 (RNF14, Accession NM\_004290) is another VGAM1654 host target gene. RNF14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF14 BINDING SITE, designated SEQ ID:10505, to the nucleotide sequence of VGAM1654 RNA, herein designated VGAM RNA, also designated SEQ ID:4365.

[55981] Another function of VGAM1654 is therefore inhibition of Ring Finger Protein 14 (RNF14, Accession NM\_004290), a gene which associates with the androgen receptor (AR); functions as a transcriptional coactivator. Accordingly, utilities of VGAM1654 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF14. The function of RNF14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827. Cat Eye Syndrome Chromo-

some Region, Candidate 1 (CECR1, Accession NM\_017424) is another VGAM1654 host target gene. CECR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CECR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CECR1 BINDING SITE, designated SEQ ID:18886, to the nucleotide sequence of VGAM1654 RNA, herein designated VGAM RNA, also designated SEQ ID:4365.

[55982] Another function of VGAM1654 is therefore inhibition of Cat Eye Syndrome Chromosome Region, Candidate 1 (CECR1, Accession NM\_017424). Accordingly, utilities of VGAM1654 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR1. KIAA1877 (Accession XM\_038616) is another VGAM1654 host target gene. KIAA1877 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1877 BINDING SITE,

designated SEQ ID:32887, to the nucleotide sequence of VGAM1654 RNA, herein designated VGAM RNA, also designated SEQ ID:4365.

[55983] Another function of VGAM1654 is therefore inhibition of KIAA1877 (Accession XM\_038616). Accordingly, utilities of VGAM1654 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1877. LOC254848 (Accession XM\_173133) is another VGAM1654 host target gene. LOC254848 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254848 BINDING SITE, designated SEQ ID:46380, to the nucleotide sequence of VGAM1654 RNA, herein designated VGAM RNA, also designated SEQ ID:4365.

[55984] Another function of VGAM1654 is therefore inhibition of LOC254848 (Accession XM\_173133). Accordingly, utilities of VGAM1654 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254848. LOC255308 (Accession XM\_170536) is another VGAM1654 host target gene. LOC255308 BINDING



SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255308 BINDING SITE, designated SEQ ID:45356, to the nucleotide sequence of VGAM1654 RNA, herein designated VGAM RNA, also designated SEQ ID:4365.

[55985] Another function of VGAM1654 is therefore inhibition of LOC255308 (Accession XM\_170536). Accordingly, utilities of VGAM1654 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255308. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1655 (VGAM1655) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[55986] VGAM1655 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1655 was detected is described hereinabove with reference to Figs. 1-8.

[55987] VGAM1655 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yellow Fever Virus.

VGAM1655 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[55988] VGAM1655 gene encodes a VGAM1655 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1655 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1655 precursor RNA is designated SEQ ID:1641, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1641 is located at position 1472 relative to the genome of Yellow Fever Virus.

[55989] VGAM1655 precursor RNA folds onto itself, forming VGAM1655 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[55990] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1655 folded precursor RNA into VGAM1655 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1655 RNA is designated SEQ ID:4366, and is provided hereinbelow with reference to the sequence listing part.

[55991] VGAM1655 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1655 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1655 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[55992] VGAM1655 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1655 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1655 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1655 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1655 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[55993] The complementary binding of VGAM1655 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1655 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1655 host target RNA into VGAM1655 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[55994] It is appreciated that VGAM1655 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1655 host target genes. The mRNA of each one of this plurality of VGAM1655 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1655 RNA, herein designated VGAM RNA, and which when bound by VGAM1655 RNA causes inhibition of translation of respective one or more VGAM1655 host target proteins.

[55995] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1655 gene, herein designated VGAM GENE, on one or more VGAM1655 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[55996] It is yet further appreciated that a function of VGAM1655 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1655 include diagnosis, prevention and treatment of viral infection by Yellow Fever Virus. Specific functions, and accordingly utilities, of VGAM1655 correlate with, and may be deduced from, the identity of the host target genes which VGAM1655 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[55997] Nucleotide sequences of the VGAM1655 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1655 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1655 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1655 are further described hereinbelow with reference to Table 1.

[55998] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1655 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1655 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[55999] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1655 gene, herein designated VGAM is inhibition of expression of VGAM1655 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1655 correlate with, and may be deduced from, the identity of the target genes which VGAM1655 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56000] FLJ12443 (Accession NM\_024830) is a VGAM1655 host target gene. FLJ12443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ12443 BINDING SITE, designated SEQ ID:24224, to the nucleotide sequence of VGAM1655 RNA, herein designated VGAM RNA, also designated SEQ ID:4366.

[56001] A function of VGAM1655 is therefore inhibition of FLJ12443 (Accession NM\_024830). Accordingly, utilities of VGAM1655 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12443. KIAA0478 (Accession NM\_014870) is another VGAM1655 host target gene. KIAA0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0478 BINDING SITE, designated SEQ ID:16980, to the nucleotide sequence of VGAM1655 RNA, herein designated VGAM RNA, also designated SEQ ID:4366.

[56002] Another function of VGAM1655 is therefore inhibition of KIAA0478 (Accession NM\_014870). Accordingly, utilities of VGAM1655 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0478. Fig. 1 further provides a conceptual descrip-



tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1656 (VGAM1656) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56003] VGAM1656 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1656 was detected is described hereinabove with reference to Figs. 1–8.

[56004] VGAM1656 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum Contagiosum Virus. VGAM1656 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56005] VGAM1656 gene encodes a VGAM1656 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1656 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1656 precursor RNA is designated SEQ ID:1642, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1642 is located at position 8730 relative to the genome of Molluscum Contagiosum Virus.

[56006] VGAM1656 precursor RNA folds onto itself, forming VGAM1656 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56007] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1656 folded precursor RNA into VGAM1656 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1656 RNA is designated SEQ ID:4367, and is provided hereinbelow with reference to the sequence listing part.

[56008] VGAM1656 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1656 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1656 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[56009] VGAM1656 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1656 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1656 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1656 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1656 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[56010] The complementary binding of VGAM1656 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1656 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1656 host target RNA into VGAM1656 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56011] It is appreciated that VGAM1656 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1656 host target genes. The mRNA of each one of this plurality of VGAM1656 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1656 RNA, herein designated VGAM RNA, and which when bound by VGAM1656 RNA causes inhibition of translation of respective one or more

VGAM1656 host target proteins.

[56012] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1656 gene, herein designated VGAM GENE, on one or more VGAM1656 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56013] It is yet further appreciated that a function of VGAM1656 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of viral infection by Molluscum Contagiosum

Virus. Specific functions, and accordingly utilities, of VGAM1656 correlate with, and may be deduced from, the identity of the host target genes which VGAM1656 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56014] Nucleotide sequences of the VGAM1656 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1656 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1656 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1656 are further described hereinbelow with reference to Table 1.

[56015] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1656 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1656 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56016] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1656 gene, herein designated VGAM is inhibition of expression of VGAM1656 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1656 correlate with, and may be deduced from, the identity of the target genes which VGAM1656 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56017] Diacylglycerol Kinase, Iota (DGKI, Accession NM\_004717) is a VGAM1656 host target gene. DGKI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGKI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKI BINDING SITE, designated SEQ ID:11079, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56018] A function of VGAM1656 is therefore inhibition of Diacylglycerol Kinase, Iota (DGKI, Accession NM\_004717), a gene which regulates the intracellular concentration of the second messenger diacylglycerol (DAG). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKI. The function of DGKI and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM1107. Hyperpolarization Activated Cyclic Nucleotide-gated Potassium Channel 2 (HCN2, Accession NM\_001194) is another VGAM1656 host target gene. HCN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCN2 BINDING SITE, designated SEQ ID:6863, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56019] Another function of VGAM1656 is therefore inhibition of Hyperpolarization Activated Cyclic Nucleotide-gated Potassium Channel 2 (HCN2, Accession NM\_001194), a gene which is hyperpolarization-activated cyclic nucleotide-gated cation channel 2 and may act as a pacemaker channel in the brain and the heart. Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCN2. The function of HCN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189. Leukemia Inhibitory Factor Re-



ceptor (LIFR, Accession NM\_002310) is another VGAM1656 host target gene. LIFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIFR BINDING SITE, designated SEQ ID:8103, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56020] Another function of VGAM1656 is therefore inhibition of Leukemia Inhibitory Factor Receptor (LIFR, Accession NM\_002310). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIFR. Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 1 (antiporter, Na<sup>+</sup>/H<sup>+</sup>, amiloride sensitive) (SLC9A1, Accession XM\_046881) is another VGAM1656 host target gene. SLC9A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC9A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of SLC9A1 BINDING SITE, designated SEQ ID:34858, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56021] Another function of VGAM1656 is therefore inhibition of Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 1 (antiporter, Na<sup>+</sup>/H<sup>+</sup>, amiloride sensitive) (SLC9A1, Accession XM\_046881), a gene which is involved in pH regulation to eliminate acids generated by active metabolism or to counter adverse environmental conditions. Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC9A1. The function of SLC9A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. SMAC (Accession NM\_138930) is another VGAM1656 host target gene. SMAC BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SMAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMAC BINDING SITE, designated SEQ ID:29050,

to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56022] Another function of VGAM1656 is therefore inhibition of SMAC (Accession NM\_138930), a gene which promotes apoptosis via caspase activation. Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMAC. The function of SMAC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Tumor Suppressing Subtransferable Candidate 4 (TSSC4, Accession NM\_005706) is another VGAM1656 host target gene. TSSC4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TSSC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSSC4 BINDING SITE, designated SEQ ID:12259, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56023] Another function of VGAM1656 is therefore inhibition of Tumor Suppressing Subtransferable Candidate 4 (TSSC4,

Accession NM\_005706), a gene which is of unknown function. Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSSC4. The function of TSSC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1233. WNT1 Inducible Signaling Pathway Protein 1 (WISP1, Accession NM\_003882) is another VGAM1656 host target gene. WISP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WISP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WISP1 BINDING SITE, designated SEQ ID:9962, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56024] Another function of VGAM1656 is therefore inhibition of WNT1 Inducible Signaling Pathway Protein 1 (WISP1, Accession NM\_003882), a gene which is a member of connective tissue growth factor family. Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

WISP1. The function of WISP1 has been established by previous studies. WNT1 (OMIM Ref. No. 164820) is a member of a family of cysteine-rich, glycosylated signaling proteins that mediate diverse developmental processes such as the control of cell proliferation, adhesion, cell polarity, and the establishment of cell fates. This family has been referred to as CCN, for connective tissue growth factor, cysteine-rich-61, neuroblastoma overexpressed. Wnt1 was identified as an oncogene activated by the insertion of mouse mammary tumor virus in virus-induced mammary adenocarcinomas. Although Wnt1 is not expressed in the normal mammary gland, expression of Wnt1 in transgenic mice causes mammary tumors. To identify downstream genes in the WNT signaling pathway that are relevant to the transformed cell phenotype, Pennica et al. (1998) used a PCR-based cDNA subtraction strategy, suppression subtractive hybridization. Pennica et al. (1998) reported the identification of 2 genes, WISP1 and WISP2 (OMIM Ref. No. 603399), that are upregulated in the mouse mammary epithelial cell line transformed by Wnt1, but not by Wnt4 (OMIM Ref. No. 603490). Together with a third related gene, WISP3 (OMIM Ref. No. 603399), these proteins define a subfamily of the

connective tissue growth factor family. Two distinct systems demonstrated WISP induction to be associated with the expression of WNT1. WISP1 genomic DNA was amplified in colon cancer cell lines and in human colon tumors and its RNA overexpressed in 84% of the tumors examined compared with patient-matched normal mucosa. WISP3 also was overexpressed in 63% of colon tumors analyzed. In contrast, WISP2 showed reduced RNA expression in 79% of the tumors. These results suggested that WISP genes may be downstream of WNT1 signaling and that aberrant levels of WISP expression in colon cancer may play a role in colon tumorigenesis. Pennica et al. (1998) found that the WISP1 cDNA encodes a 367-amino acid protein. Mouse and human WISP1 proteins are 84% identical; both have hydrophobic N-terminal signal sequences, 38 conserved cysteine residues, and 4 potential N-linked glycosylation sites. Alignment of the 3 human WISP proteins showed that WISP1 and WISP3 are most similar (42%), whereas WISP2 had 37% identity with WISP1 and 32% identity with WISP3. Tanaka et al. (2001) used targeted differential displays to identify a novel variant of WISP1, designated WISP1v, which was overexpressed in scirrhous gastric carcinomas. The predicted protein of the

variant WISP1 completely lacks a module of von Willebrand factor type C (see OMIM Ref. No. 193400) that is thought to participate in protein complex formation. Ectopic expression of the variant showed it to be a secreted oncoprotein inducing a striking cellular transformation and rapid piling-up growth. The authors noted that WISP1 transfectants enhanced the invasive phenotype of cocultured gastric carcinoma cells, while wildtype WISP1 had no such potential. By use of radiation hybrid mapping panels, Pennica et al. (1998) mapped the 3 WISP genes. WISP1 was mapped to 8q24.1–q24.3, roughly 4 Mb distal to MYC (OMIM Ref. No. 190080). WISP2 was mapped to 20q12–q13.1, and WISP3 to 6q22–q23.

[56025] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56026] Pennica, D.; Swanson, T. A.; Welsh, J. W.; Roy, M. A.; Lawrence, D. A.; Lee, J.; Brush, J.; Taneyhill, L. A.; Deuel, B.; Lew, M.; Watanabe, C.; Cohen, R. L.; Melhem, M. F.; Finley, G. G.; Quirke, P.; Goddard, A. D.; Hillan, K. J.; Gurney, A. L.; Botstein, D.; Levine, A. J. : WISP genes are members of the connective tissue growth factor family that are up-regulated in Wnt-1-transformed cells and

aberrantly expressed in human colon tumors. Proc. Nat. Acad. Sci. 95: 14717–14722, 1998. ; and

[56027] Tanaka, S.; Sugimachi, K.; Saeki, H.; Kinoshita, J.; Ohga, T.; Shimada, M.; Maehara, Y.; Sugimachi, K. : A novel variant of WISP1 lacking a von Willebrand type C module overexpressed in.

[56028] Further studies establishing the function and utilities of WISP1 are found in John Hopkins OMIM database record ID 603398, and in cited publications numbered 7621–7622 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 22 Open Reading Frame 2 (C22orf2, Accession XM\_170492) is another VGAM1656 host target gene. C22orf2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C22orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf2 BINDING SITE, designated SEQ ID:45334, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56029] Another function of VGAM1656 is therefore inhibition of Chromosome 22 Open Reading Frame 2 (C22orf2, Acces-



sion XM\_170492). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf2. FLJ00001 (Accession XM\_088525) is another VGAM1656 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00001 BINDING SITE, designated SEQ ID:39775, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56030] Another function of VGAM1656 is therefore inhibition of FLJ00001 (Accession XM\_088525). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00001. FLJ22037 (Accession XM\_168215) is another VGAM1656 host target gene. FLJ22037 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22037, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ22037 BINDING SITE, designated SEQ ID:45075, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56031] Another function of VGAM1656 is therefore inhibition of FLJ22037 (Accession XM\_168215). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22037. Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM\_029962) is another VGAM1656 host target gene. KCNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNT1 BINDING SITE, designated SEQ ID:30977, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56032] Another function of VGAM1656 is therefore inhibition of Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM\_029962). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with KCNT1. MDS018 (Accession NM\_021823) is another VGAM1656 host target gene. MDS018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MDS018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MDS018 BINDING SITE, designated SEQ ID:22401, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56033] Another function of VGAM1656 is therefore inhibition of MDS018 (Accession NM\_021823). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MDS018. Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654) is another VGAM1656 host target gene. SDC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC3 BINDING SITE, designated SEQ ID:16083,

to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56034] Another function of VGAM1656 is therefore inhibition of Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC3. LOC126353 (Accession XM\_059034) is another VGAM1656 host target gene. LOC126353 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126353, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126353 BINDING SITE, designated SEQ ID:36829, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56035] Another function of VGAM1656 is therefore inhibition of LOC126353 (Accession XM\_059034). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126353. LOC128989 (Accession XM\_059310) is another VGAM1656 host target gene. LOC128989 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128989 BINDING SITE, designated SEQ ID:36940, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56036] Another function of VGAM1656 is therefore inhibition of LOC128989 (Accession XM\_059310). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128989. LOC134265 (Accession XM\_059702) is another VGAM1656 host target gene. LOC134265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC134265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134265 BINDING SITE, designated SEQ ID:37074, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56037] Another function of VGAM1656 is therefore inhibition of

LOC134265 (Accession XM\_059702). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134265. LOC157349 (Accession XM\_088298) is another VGAM1656 host target gene. LOC157349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157349 BINDING SITE, designated SEQ ID:39599, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56038] Another function of VGAM1656 is therefore inhibition of LOC157349 (Accession XM\_088298). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157349. LOC219700 (Accession XM\_167570) is another VGAM1656 host target gene. LOC219700 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC219700 BINDING SITE, designated SEQ ID:44701, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56039] Another function of VGAM1656 is therefore inhibition of LOC219700 (Accession XM\_167570). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219700. LOC221399 (Accession XM\_168134) is another VGAM1656 host target gene. LOC221399 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221399 BINDING SITE, designated SEQ ID:45051, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56040] Another function of VGAM1656 is therefore inhibition of LOC221399 (Accession XM\_168134). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221399. LOC256158 (Accession XM\_175125) is an-

other VGAM1656 host target gene. LOC256158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE, designated SEQ ID:46625, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56041] Another function of VGAM1656 is therefore inhibition of LOC256158 (Accession XM\_175125). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256158. LOC51337 (Accession NM\_016647) is another VGAM1656 host target gene. LOC51337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51337 BINDING SITE, designated SEQ ID:18765, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.



[56042] Another function of VGAM1656 is therefore inhibition of LOC51337 (Accession NM\_016647). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51337. LOC54103 (Accession XM\_168508) is another VGAM1656 host target gene. LOC54103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC54103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC54103 BINDING SITE, designated SEQ ID:45208, to the nucleotide sequence of VGAM1656 RNA, herein designated VGAM RNA, also designated SEQ ID:4367.

[56043] Another function of VGAM1656 is therefore inhibition of LOC54103 (Accession XM\_168508). Accordingly, utilities of VGAM1656 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC54103. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1657 (VGAM1657) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[56044] VGAM1657 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1657 was detected is described hereinabove with reference to Figs. 1-8.

[56045] VGAM1657 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Mollusum Contagiosum Virus. VGAM1657 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56046] VGAM1657 gene encodes a VGAM1657 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1657 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1657 precursor RNA is designated SEQ ID:1643, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1643 is located at position 9944 relative to the genome of Mollusum Contagiosum Virus.

[56047] VGAM1657 precursor RNA folds onto itself, forming VGAM1657 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56048] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1657 folded precursor RNA into VGAM1657 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1657 RNA is designated SEQ ID:4368, and is provided hereinbelow with reference to the sequence listing part.

[56049] VGAM1657 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1657 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1657 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56050] VGAM1657 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1657 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1657 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1657 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1657 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56051] The complementary binding of VGAM1657 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1657 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1657 host target RNA into VGAM1657 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56052] It is appreciated that VGAM1657 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1657 host target genes. The mRNA of each one of this plurality of VGAM1657 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1657 RNA, herein designated VGAM RNA, and which when bound by VGAM1657 RNA causes inhibition of translation of respective one or more VGAM1657 host target proteins.

[56053] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1657 gene, herein designated VGAM GENE, on one or more VGAM1657 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56054] It is yet further appreciated that a function of VGAM1657 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1657 include diagnosis, prevention and treatment of viral infection by Molluscum Contagiosum Virus. Specific functions, and accordingly utilities, of VGAM1657 correlate with, and may be deduced from, the identity of the host target genes which VGAM1657 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[56055] Nucleotide sequences of the VGAM1657 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1657 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1657 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1657 are further described hereinbelow with reference to Table 1.

[56056] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1657 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1657 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56057] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1657 gene, herein designated VGAM is inhibition of expression of VGAM1657 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1657 correlate with, and may be deduced from, the identity of the target genes which VGAM1657 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56058] MAP/microtubule Affinity-regulating Kinase 3 (MARK3, Accession NM\_002376) is a VGAM1657 host target gene. MARK3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MARK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MARK3 BINDING SITE, designated SEQ ID:8191, to the nucleotide sequence of VGAM1657 RNA, herein designated VGAM RNA, also designated SEQ ID:4368.

[56059] A function of VGAM1657 is therefore inhibition of MAP/ microtubule Affinity-regulating Kinase 3 (MARK3, Accession NM\_002376), a gene which may be involved in cell cycle regulation. Accordingly, utilities of VGAM1657 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MARK3. The function of MARK3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM964.FLJ21276 (Accession NM\_024633) is another VGAM1657 host target gene. FLJ21276 BINDING SITE is HOST TARGET binding site found in the 3` untranslated



region of mRNA encoded by FLJ21276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21276 BINDING SITE, designated SEQ ID:23901, to the nucleotide sequence of VGAM1657 RNA, herein designated VGAM RNA, also designated SEQ ID:4368.

[56060] Another function of VGAM1657 is therefore inhibition of FLJ21276 (Accession NM\_024633). Accordingly, utilities of VGAM1657 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21276. LOC92299 (Accession XM\_044075) is another VGAM1657 host target gene. LOC92299 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92299 BINDING SITE, designated SEQ ID:34130, to the nucleotide sequence of VGAM1657 RNA, herein designated VGAM RNA, also designated SEQ ID:4368.

[56061] Another function of VGAM1657 is therefore inhibition of LOC92299 (Accession XM\_044075). Accordingly, utilities of VGAM1657 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92299. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1658 (VGAM1658) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56062] VGAM1658 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1658 was detected is described hereinabove with reference to Figs. 1–8.

[56063] VGAM1658 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum Contagiosum Virus. VGAM1658 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56064] VGAM1658 gene encodes a VGAM1658 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1658 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1658 precursor RNA is designated SEQ ID:1644, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1644 is located at position 9453 relative to the genome of Molluscum Contagiosum Virus.

[56065] VGAM1658 precursor RNA folds onto itself, forming VGAM1658 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56066] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1658 folded precursor RNA into VGAM1658 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1658 RNA is designated SEQ ID:4369, and is provided hereinbelow with reference to the sequence listing part.

[56067] VGAM1658 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1658 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1658 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[56068] VGAM1658 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1658 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1658 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1658 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1658 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56069] The complementary binding of VGAM1658 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1658 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1658 host target RNA into VGAM1658 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56070] It is appreciated that VGAM1658 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1658 host target genes. The mRNA of each one of this plurality of VGAM1658 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1658 RNA, herein designated VGAM RNA, and which when bound by VGAM1658 RNA causes inhibition of translation of respective one or more VGAM1658 host target proteins.

[56071] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1658 gene, herein designated VGAM GENE, on one or more VGAM1658 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56072] It is yet further appreciated that a function of VGAM1658 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGAM1658 correlate with, and may be deduced from, the identity of the host target genes which VGAM1658 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56073] Nucleotide sequences of the VGAM1658 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1658 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1658 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1658 are further described hereinbelow with reference to Table 1.

[56074] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1658 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1658 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[56075] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1658 gene, herein designated VGAM is inhibition of expression of VGAM1658 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1658 correlate with, and may be deduced from, the identity of the target genes which VGAM1658 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56076] Ras Homolog Gene Family, Member C (ARHC, Accession NM\_005167) is a VGAM1658 host target gene. ARHC BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARHC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHC BINDING SITE, designated SEQ ID:11663, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56077] A function of VGAM1658 is therefore inhibition of Ras Homolog Gene Family, Member C (ARHC, Accession NM\_005167), a gene which remodels of the actin cytoskeleton during cell morphogenesis and motility. Ac-



cordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHC. The function of ARHC and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM885. Histone Deacetylase 4 (HDAC4, Accession NM\_006037) is another VGAM1658 host target gene. HDAC4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HDAC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC4 BINDING SITE, designated SEQ ID:12665, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56078] Another function of VGAM1658 is therefore inhibition of Histone Deacetylase 4 (HDAC4, Accession NM\_006037), a gene which is responsible for the deacetylation of lysine residues on the n-terminal part of the core histones and may mediate transcriptional regulation. Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with HDAC4. The function of HDAC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM264. Inducible T-cell Co-stimulator (ICOS, Accession NM\_012092) is another VGAM1658 host target gene. ICOS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICOS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICOS BINDING SITE, designated SEQ ID:14391, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56079] Another function of VGAM1658 is therefore inhibition of Inducible T-cell Co-stimulator (ICOS, Accession NM\_012092), a gene which forms homodimers and functions as an inducible T-cell co-stimulator. Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICOS. The function of ICOS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM18.LIM Domains Containing 1 (LIMD1, Accession NM\_014240) is another VGAM1658 host target gene. LIMD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LIMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMD1 BINDING SITE, designated SEQ ID:15501, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56080] Another function of VGAM1658 is therefore inhibition of LIM Domains Containing 1 (LIMD1, Accession NM\_014240). Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMD1. ASAH (Accession NM\_004315) is another VGAM1658 host target gene. ASAH BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ASAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASAH BINDING SITE, designated SEQ ID:10518,

to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56081] Another function of VGAM1658 is therefore inhibition of ASAH (Accession NM\_004315). Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASAH. KIAA0934 (Accession XM\_034536) is another VGAM1658 host target gene. KIAA0934 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0934 BINDING SITE, designated SEQ ID:32121, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56082] Another function of VGAM1658 is therefore inhibition of KIAA0934 (Accession XM\_034536). Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0934. KIAA1904 (Accession XM\_056282) is another VGAM1658 host target gene. KIAA1904 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1904, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1904 BINDING SITE, designated SEQ ID:36383, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56083] Another function of VGAM1658 is therefore inhibition of KIAA1904 (Accession XM\_056282). Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1904. LIP8 (Accession XM\_113928) is another VGAM1658 host target gene. LIP8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LIP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIP8 BINDING SITE, designated SEQ ID:42547, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56084] Another function of VGAM1658 is therefore inhibition of LIP8 (Accession XM\_113928). Accordingly, utilities of

VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIP8. LOC149478 (Accession XM\_086536) is another VGAM1658 host target gene. LOC149478 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149478 BINDING SITE, designated SEQ ID:38751, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56085] Another function of VGAM1658 is therefore inhibition of LOC149478 (Accession XM\_086536). Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149478. LOC196477 (Accession XM\_113728) is another VGAM1658 host target gene. LOC196477 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC196477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC196477 BINDING SITE, designated SEQ ID:42376, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56086] Another function of VGAM1658 is therefore inhibition of LOC196477 (Accession XM\_113728). Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196477. LOC199990 (Accession XM\_114083) is another VGAM1658 host target gene. LOC199990 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199990, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199990 BINDING SITE, designated SEQ ID:42682, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56087] Another function of VGAM1658 is therefore inhibition of LOC199990 (Accession XM\_114083). Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199990. LOC245806 (Accession XM\_166309) is another VGAM1658 host target gene. LOC245806 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC245806, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245806 BINDING SITE, designated SEQ ID:44132, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56088] Another function of VGAM1658 is therefore inhibition of LOC245806 (Accession XM\_166309). Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245806. LOC91663 (Accession NM\_138373) is another VGAM1658 host target gene. LOC91663 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91663 BINDING SITE, designated SEQ ID:28753, to the nucleotide sequence of VGAM1658 RNA, herein designated VGAM RNA, also designated SEQ ID:4369.

[56089] Another function of VGAM1658 is therefore inhibition of



LOC91663 (Accession NM\_138373). Accordingly, utilities of VGAM1658 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91663. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1659 (VGAM1659) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56090] VGAM1659 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1659 was detected is described hereinabove with reference to Figs. 1-8.

[56091] VGAM1659 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum Contagiosum Virus. VGAM1659 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56092] VGAM1659 gene encodes a VGAM1659 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1659 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1659 precursor RNA is designated SEQ ID:1645, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1645 is located at position 13023 relative to the genome of Molluscum Contagiosum Virus.

[56093] VGAM1659 precursor RNA folds onto itself, forming VGAM1659 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56094] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1659 folded precursor RNA into VGAM1659 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide se-

quence of VGAM1659 RNA is designated SEQ ID:4370, and is provided hereinbelow with reference to the sequence listing part.

[56095] VGAM1659 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1659 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1659 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56096] VGAM1659 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1659 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1659 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1659 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1659 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[56097] The complementary binding of VGAM1659 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1659 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1659 host target RNA into VGAM1659 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56098] It is appreciated that VGAM1659 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1659 host target genes. The mRNA of each one of this plurality of VGAM1659 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1659 RNA, herein designated VGAM RNA, and which when bound by VGAM1659 RNA causes inhibition of translation of respective one or more VGAM1659 host target proteins.

[56099] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1659 gene, herein designated VGAM GENE, on one or more VGAM1659 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56100] It is yet further appreciated that a function of VGAM1659

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGAM1659 correlate with, and may be deduced from, the identity of the host target genes which VGAM1659 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56101] Nucleotide sequences of the VGAM1659 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1659 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1659 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1659 are further described hereinbelow with reference to Table 1.

[56102] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1659 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1659 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56103] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1659 gene, herein designated VGAM is inhibition of expression of VGAM1659 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1659 correlate with, and may be deduced from, the identity of the target genes which VGAM1659 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56104] Egl Nine Homolog 2 (*C. elegans*) (EGLN2, Accession NM\_080732) is a VGAM1659 host target gene. EGLN2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGLN2 BINDING SITE, designated SEQ ID:28021, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56105] A function of VGAM1659 is therefore inhibition of Egl Nine Homolog 2 (*C. elegans*) (EGLN2, Accession NM\_080732), a gene which is an essential component of the pathway. Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with EGLN2. The function of EGLN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM432. Early Growth Response 4 (EGR4, Accession NM\_001965) is another VGAM1659 host target gene. EGR4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGR4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGR4 BINDING SITE, designated SEQ ID:7693, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56106] Another function of VGAM1659 is therefore inhibition of Early Growth Response 4 (EGR4, Accession NM\_001965), a gene which is a Member of the early-response-gene family. Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGR4. The function of EGR4 has been established by previous studies. When eukaryotic cells are stimulated to undergo mitogenesis or differentiation, the expression of a small subset of genes, termed



early response or immediate early genes, is rapidly activated. Many early response genes encode transcriptional regulators, for example, nerve growth factor-induced clones C and A, also called EGR4 and EGR1 (OMIM Ref. No. 128990), respectively. By use of fluorescence in situ hybridization, Crosby et al. (1992) localized the human EGR4 gene to 2p13. Barrow et al. (1994) demonstrated that the homologous gene in the mouse (Egr4) maps to chromosome 6 in a region of conserved homology of synteny with human chromosome 2.

[56107] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56108] Barrow, L. L.; Simin, K.; Jones, J. M.; Lee, D. C.; Meisler, M. H. : Conserved linkage of early growth response 4, annexin 4, and transforming growth factor alpha on mouse chromosome 6. *Genomics* 19: 388–390, 1994. ; and

[56109] Crosby, S. D.; Veile, R. A.; Donis-Keller, H.; Baraban, J. M.; Bhat, R. V.; Simburger, K. S.; Milbrandt, J. : Neural-specific expression, genomic structure, and chromosomal localization.

[56110] Further studies establishing the function and utilities of EGR4 are found in John Hopkins OMIM database record ID

128992, and in cited publications numbered 11668–11669 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myxovirus (influenza virus) Resistance 1, Interferon-inducible Protein P78 (mouse) (MX1, Accession NM\_002462) is another VGAM1659 host target gene. MX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MX1 BINDING SITE, designated SEQ ID:8292, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56111] Another function of VGAM1659 is therefore inhibition of Myxovirus (influenza virus) Resistance 1, Interferon-inducible Protein P78 (mouse) (MX1, Accession NM\_002462), a gene which is responsible for a specific antiviral state against influenza virus infection. Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MX1. The function of MX1 and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM973. Transducin (beta)-like 1X-linked (TBL1X, Accession NM\_005647) is another VGAM1659 host target gene. TBL1X BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBL1X, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBL1X BINDING SITE, designated SEQ ID:12180, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56112] Another function of VGAM1659 is therefore inhibition of Transducin (beta)-like 1X-linked (TBL1X, Accession NM\_005647), a gene which activates latent HDAC3 activity. Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBL1X. The function of TBL1X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1151. ATPW (Accession NM\_015684) is another VGAM1659 host target gene. ATPW BINDING SITE is HOST TARGET binding site

found in the 5' untranslated region of mRNA encoded by ATPW, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATPW BINDING SITE, designated SEQ ID:17908, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56113] Another function of VGAM1659 is therefore inhibition of ATPW (Accession NM\_015684). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATPW. Chemokine (C-C motif) Receptor 1 (CCR1, Accession NM\_001295) is another VGAM1659 host target gene. CCR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR1 BINDING SITE, designated SEQ ID:6974, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56114] Another function of VGAM1659 is therefore inhibition of Chemokine (C-C motif) Receptor 1 (CCR1, Accession

NM\_001295). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR1. FLJ12552 (Accession NM\_022832) is another VGAM1659 host target gene.

FLJ12552 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12552, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12552 BINDING SITE, designated SEQ ID:23115, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56115] Another function of VGAM1659 is therefore inhibition of FLJ12552 (Accession NM\_022832). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12552. FLJ20306 (Accession NM\_017756) is another VGAM1659 host target gene. FLJ20306 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ20306 BINDING SITE, designated SEQ ID:19368, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56116] Another function of VGAM1659 is therefore inhibition of FLJ20306 (Accession NM\_017756). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20306. FLJ32865 (Accession NM\_144613) is another VGAM1659 host target gene. FLJ32865 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32865 BINDING SITE, designated SEQ ID:29424, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56117] Another function of VGAM1659 is therefore inhibition of FLJ32865 (Accession NM\_144613). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32865. KIAA1910 (Accession XM\_055514) is another

VGAM1659 host target gene. KIAA1910 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1910 BINDING SITE, designated SEQ ID:36288, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56118] Another function of VGAM1659 is therefore inhibition of KIAA1910 (Accession XM\_055514). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1910. LOC143888 (Accession XM\_084669) is another VGAM1659 host target gene. LOC143888 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143888, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143888 BINDING SITE, designated SEQ ID:37668, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56119] Another function of VGAM1659 is therefore inhibition of LOC143888 (Accession XM\_084669). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143888. LOC157737 (Accession XM\_098819) is another VGAM1659 host target gene. LOC157737 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157737 BINDING SITE, designated SEQ ID:41842, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56120] Another function of VGAM1659 is therefore inhibition of LOC157737 (Accession XM\_098819). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157737. LOC158310 (Accession XM\_098919) is another VGAM1659 host target gene. LOC158310 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158310, corresponding to a HOST TARGET binding site such as BIND-



ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158310 BINDING SITE, designated SEQ ID:41948, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56121] Another function of VGAM1659 is therefore inhibition of LOC158310 (Accession XM\_098919). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158310. LOC163033 (Accession XM\_091949) is another VGAM1659 host target gene. LOC163033 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163033, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163033 BINDING SITE, designated SEQ ID:40073, to the nucleotide sequence of VGAM1659 RNA, herein designated VGAM RNA, also designated SEQ ID:4370.

[56122] Another function of VGAM1659 is therefore inhibition of LOC163033 (Accession XM\_091949). Accordingly, utilities of VGAM1659 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC163033. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1660 (VGAM1660) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56123] VGAM1660 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1660 was detected is described hereinabove with reference to Figs. 1–8.

[56124] VGAM1660 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum Contagiosum Virus. VGAM1660 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56125] VGAM1660 gene encodes a VGAM1660 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1660 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1660 precursor RNA is designated SEQ ID:1646, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1646 is located at position 5477 relative to the genome of Molluscum Contagiosum Virus.

- [56126] VGAM1660 precursor RNA folds onto itself, forming VGAM1660 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [56127] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1660 folded precursor RNA into VGAM1660 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1660 RNA is designated SEQ ID:4371, and is provided hereinbelow with reference to the sequence listing part.

[56128] VGAM1660 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1660 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1660 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56129] VGAM1660 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1660 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1660 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1660 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1660 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56130] The complementary binding of VGAM1660 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1660 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1660 host target RNA into VGAM1660 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56131] It is appreciated that VGAM1660 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1660 host target genes. The mRNA of each one of this plurality of VGAM1660 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1660 RNA, herein designated VGAM RNA, and which when bound by VGAM1660 RNA causes

inhibition of translation of respective one or more VGAM1660 host target proteins.

[56132] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1660 gene, herein designated VGAM GENE, on one or more VGAM1660 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56133] It is yet further appreciated that a function of VGAM1660 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1660 include diagnosis, prevention and

treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGAM1660 correlate with, and may be deduced from, the identity of the host target genes which VGAM1660 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56134] Nucleotide sequences of the VGAM1660 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1660 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1660 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1660 are further described hereinbelow with reference to Table 1.

[56135] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1660 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1660 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56136] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1660 gene, herein designated VGAM is inhibition of expression of VGAM1660 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1660 correlate with, and may be deduced from, the identity of the target genes which VGAM1660 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56137] BTG Family, Member 2 (BTG2, Accession NM\_006763) is a VGAM1660 host target gene. BTG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTG2 BINDING SITE, designated SEQ ID:13621, to the nucleotide sequence of VGAM1660 RNA, herein designated VGAM RNA, also designated SEQ ID:4371.

[56138] A function of VGAM1660 is therefore inhibition of BTG Family, Member 2 (BTG2, Accession NM\_006763). Accordingly, utilities of VGAM1660 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTG2. Casein Kinase 1, Gamma 1 (CSNK1G1, Accession NM\_022048) is another VGAM1660 host target gene. CSNK1G1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded



by CSNK1G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSNK1G1 BINDING SITE, designated SEQ ID:22568, to the nucleotide sequence of VGAM1660 RNA, herein designated VGAM RNA, also designated SEQ ID:4371.

[56139] Another function of VGAM1660 is therefore inhibition of Casein Kinase 1, Gamma 1 (CSNK1G1, Accession NM\_022048). Accordingly, utilities of VGAM1660 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSNK1G1. KIAA0528 (Accession XM\_051454) is another VGAM1660 host target gene. KIAA0528 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0528, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0528 BINDING SITE, designated SEQ ID:35840, to the nucleotide sequence of VGAM1660 RNA, herein designated VGAM RNA, also designated SEQ ID:4371.

[56140] Another function of VGAM1660 is therefore inhibition of

KIAA0528 (Accession XM\_051454). Accordingly, utilities of VGAM1660 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0528. KIAA0987 (Accession NM\_012307) is another VGAM1660 host target gene. KIAA0987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0987 BINDING SITE, designated SEQ ID:14674, to the nucleotide sequence of VGAM1660 RNA, herein designated VGAM RNA, also designated SEQ ID:4371.

[56141] Another function of VGAM1660 is therefore inhibition of KIAA0987 (Accession NM\_012307). Accordingly, utilities of VGAM1660 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0987. KIAA1117 (Accession XM\_028219) is another VGAM1660 host target gene. KIAA1117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1117 BINDING SITE, designated SEQ ID:30634, to the nucleotide sequence of VGAM1660 RNA, herein designated VGAM RNA, also designated SEQ ID:4371.

[56142] Another function of VGAM1660 is therefore inhibition of KIAA1117 (Accession XM\_028219). Accordingly, utilities of VGAM1660 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1117. LOC149146 (Accession XM\_086441) is another VGAM1660 host target gene. LOC149146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149146 BINDING SITE, designated SEQ ID:38656, to the nucleotide sequence of VGAM1660 RNA, herein designated VGAM RNA, also designated SEQ ID:4371.

[56143] Another function of VGAM1660 is therefore inhibition of LOC149146 (Accession XM\_086441). Accordingly, utilities of VGAM1660 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149146. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1661 (VGAM1661) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56144] VGAM1661 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1661 was detected is described hereinabove with reference to Figs. 1–8.

[56145] VGAM1661 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1661 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56146] VGAM1661 gene encodes a VGAM1661 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1661 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1661 precursor RNA is designated SEQ ID:1647, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1647 is located at position 100245 relative to the genome of Cercopithecine Herpesvirus 7.

[56147] VGAM1661 precursor RNA folds onto itself, forming VGAM1661 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56148] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1661 folded precursor RNA into VGAM1661 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1661 RNA is designated SEQ ID:4372, and is provided hereinbelow with reference to the sequence listing part.

[56149] VGAM1661 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1661 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1661 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[56150] VGAM1661 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1661 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1661 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1661 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1661 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[56151] The complementary binding of VGAM1661 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1661 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1661 host target RNA into VGAM1661 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56152] It is appreciated that VGAM1661 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1661 host target genes. The mRNA of each one of this plurality of VGAM1661 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1661 RNA, herein designated VGAM RNA, and which when bound by VGAM1661 RNA causes inhibition of translation of respective one or more

VGAM1661 host target proteins.

[56153] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1661 gene, herein designated VGAM GENE, on one or more VGAM1661 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56154] It is yet further appreciated that a function of VGAM1661 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1661 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus



7. Specific functions, and accordingly utilities, of VGAM1661 correlate with, and may be deduced from, the identity of the host target genes which VGAM1661 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56155] Nucleotide sequences of the VGAM1661 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1661 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1661 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1661 are further described hereinbelow with reference to Table 1.

[56156] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1661 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1661 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56157] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1661 gene, herein designated VGAM is inhibition of expression of VGAM1661 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1661 correlate with, and may be deduced from, the identity of the target genes which VGAM1661 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56158] Ephrin-A5 (EFNA5, Accession NM\_001962) is a VGAM1661 host target gene. EFNA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNA5 BINDING SITE, designated SEQ ID:7683, to the nucleotide sequence of VGAM1661 RNA, herein designated VGAM RNA, also designated SEQ ID:4372.

[56159] A function of VGAM1661 is therefore inhibition of Ephrin-A5 (EFNA5, Accession NM\_001962). Accordingly, utilities of VGAM1661 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNA5. LOC151445 (Accession XM\_045283) is another VGAM1661 host target gene. LOC151445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151445, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151445 BINDING SITE, designated SEQ ID:34418, to the nucleotide sequence of VGAM1661 RNA, herein designated VGAM RNA, also designated SEQ ID:4372.

[56160] Another function of VGAM1661 is therefore inhibition of LOC151445 (Accession XM\_045283). Accordingly, utilities of VGAM1661 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151445. LOC161635 (Accession XM\_172921) is another VGAM1661 host target gene. LOC161635 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC161635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161635 BINDING SITE, designated SEQ ID:46183, to the nucleotide sequence of VGAM1661 RNA, herein designated VGAM RNA, also designated SEQ ID:4372.

[56161] Another function of VGAM1661 is therefore inhibition of LOC161635 (Accession XM\_172921). Accordingly, utilities of VGAM1661 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC161635. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1662 (VGAM1662) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56162] VGAM1662 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1662 was detected is described hereinabove with reference to Figs. 1–8.

[56163] VGAM1662 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1662 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56164] VGAM1662 gene encodes a VGAM1662 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1662 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1662 precursor RNA is designated SEQ ID:1648, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1648 is located at position 99606 relative to the genome of Cercopithecine Herpesvirus 7.

- [56165] VGAM1662 precursor RNA folds onto itself, forming VGAM1662 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [56166] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1662 folded precursor RNA into VGAM1662 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1662 RNA is designated SEQ ID:4373, and is provided hereinbelow with reference to the sequence listing part.

[56167] VGAM1662 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1662 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1662 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56168] VGAM1662 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1662 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1662 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1662 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1662 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56169] The complementary binding of VGAM1662 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1662 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1662 host target RNA into VGAM1662 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56170] It is appreciated that VGAM1662 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1662 host target genes. The mRNA of each one of this plurality of VGAM1662 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1662 RNA, herein designated VGAM RNA, and which when bound by VGAM1662 RNA causes

inhibition of translation of respective one or more VGAM1662 host target proteins.

[56171] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1662 gene, herein designated VGAM GENE, on one or more VGAM1662 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56172] It is yet further appreciated that a function of VGAM1662 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1662 include diagnosis, prevention and



treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1662 correlate with, and may be deduced from, the identity of the host target genes which VGAM1662 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56173] Nucleotide sequences of the VGAM1662 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1662 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1662 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1662 are further described hereinbelow with reference to Table 1.

[56174] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1662 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1662 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56175] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1662 gene, herein designated VGAM is inhibition of expression of VGAM1662 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1662 correlate with, and may be deduced from, the identity of the target genes which VGAM1662 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56176] Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM\_004393) is a VGAM1662 host target gene. DAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAG1 BINDING SITE, designated SEQ ID:10635, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56177] A function of VGAM1662 is therefore inhibition of Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM\_004393), a gene which may provide linkage between the sarcolemma and extracellular matrix (ECM). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAG1. The function of DAG1 and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM1095. Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM\_005463) is another VGAM1662 host target gene. HNRPDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPDL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPDL BINDING SITE, designated SEQ ID:11951, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56178] Another function of VGAM1662 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM\_005463), a gene which binds to rna molecules that contain au-rich elements. Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPDL. The function of HNRPDL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. Phosphodiesterase 7A

(PDE7A, Accession XM\_037534) is another VGAM1662 host target gene. PDE7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE7A BINDING SITE, designated SEQ ID:32641, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56179] Another function of VGAM1662 is therefore inhibition of Phosphodiesterase 7A (PDE7A, Accession XM\_037534), a gene which is a CAMP-specific phosphodiesterase 7A and plays a role in signal transduction. Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE7A. The function of PDE7A has been established by previous studies. Cyclic nucleotides serve as second messengers that mediate a variety of cellular responses to extracellular signals such as hormones, light, and neurotransmitters. Cyclic nucleotide phosphodiesterases (PDEs) play a role in signal transduction by regulating the cellular concentrations of cyclic nucleotides. Mammalian cells contain

multiple PDEs that are distinguished into at least 7 families based on their substrate affinity and on their selective sensitivity to cofactors and inhibitory drugs. These families are: (I)  $\text{Ca}^{2+}$ /calmodulin-dependent PDEs; (II) cGMP-stimulated PDEs; (III) cGMP-inhibited PDEs; (IV) cAMP-specific PDEs; (V) cGMP-specific PDEs; (VI) photoreceptor PDEs; and (VII) high-affinity, cAMP-specific. From the amino acid sequences, it is evident that all these PDE families contain a related domain, thought to be the catalytic domain, with approximately 30% sequence identity between families. Members of the same family are more closely related; they share 60 to 80% sequence identity throughout the entire coding region. Michaeli et al. (1993) established a highly sensitive functional screen for the isolation of cDNAs encoding cAMP phosphodiesterases by complementation of defects in the *Saccharomyces cerevisiae* strain lacking both endogenous cAMP PDE genes, PDE1 and PDE2. Three groups of cDNAs corresponding to 3 distinct human genes encoding cAMP-specific PDEs were isolated from a human glioblastoma cDNA library using this functional screen. Two of the genes were closely related to the *Drosophila* 'dunce' cAMP-specific PDE. The third gene, which Michaeli et al. (1993) referred

to as HCP1, encoded a novel cAMP-specific PDE. HCP1 had an amino acid sequence related to the sequences of the catalytic domains of all cyclic nucleotide PDEs. It is a high-affinity cAMP-specific PDE that does not share other properties of the cAMP-specific PDE family, however. The PDE activity of HCP1 was not sensitive to cGMP or other inhibitors of the cGMP-inhibitable PDEs. The biochemical and pharmacologic properties of HCP1 suggested to Michaeli et al. (1993) that it is a member of a previously undiscovered cyclic nucleotide PDE family, which they designated as family VII. Northern blot analysis indicated the presence of high levels of an HCP1 mRNA in human skeletal muscle.

[56180] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56181] Han, P.; Fletcher, C. F.; Copeland, N. G.; Jenkins, N. A.; Yaremko, L. M.; Michaeli, T. : Assignment of the mouse Pde7A gene to the proximal region of chromosome 3 and of the human PDE7A gene to chromosome 8q13. *Genomics* 48: 275-276, 1998. ; and

[56182] Michaeli, T.; Bloom, T. J.; Martins, T.; Loughney, K.; Ferguson, K.; Riggs, M.; Rodgers, L.; Beavo, J. A.; Wigler, M. :

Isolation and characterization of a previously undetected human c.

[56183] Further studies establishing the function and utilities of PDE7A are found in John Hopkins OMIM database record ID 171885, and in cited publications numbered 12443–12445 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ret Finger Protein (RFP, Accession NM\_006510) is another VGAM1662 host target gene. RFP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RFP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFP BINDING SITE, designated SEQ ID:13262, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56184] Another function of VGAM1662 is therefore inhibition of Ret Finger Protein (RFP, Accession NM\_006510), a gene which involves in transcriptional regulation and may act in male germ cell development. Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFP.

The function of RFP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM302.DKFZp434G179 (Accession XM\_087065) is another VGAM1662 host target gene. DKFZp434G179 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp434G179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434G179 BINDING SITE, designated SEQ ID:39044, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56185] Another function of VGAM1662 is therefore inhibition of DKFZp434G179 (Accession XM\_087065). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434G179. Family with Sequence Similarity 8, Member A1 (FAM8A1, Accession NM\_016255) is another VGAM1662 host target gene. FAM8A1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FAM8A1, corresponding to a



HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FAM8A1 BINDING SITE, designated SEQ ID:18382, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56186] Another function of VGAM1662 is therefore inhibition of Family with Sequence Similarity 8, Member A1 (FAM8A1, Accession NM\_016255). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAM8A1. FLJ13456 (Accession XM\_038291) is another VGAM1662 host target gene. FLJ13456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13456 BINDING SITE, designated SEQ ID:32799, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56187] Another function of VGAM1662 is therefore inhibition of FLJ13456 (Accession XM\_038291). Accordingly, utilities of

VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13456. KIAA1189 (Accession XM\_050508) is another VGAM1662 host target gene. KIAA1189 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1189 BINDING SITE, designated SEQ ID:35653, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56188] Another function of VGAM1662 is therefore inhibition of KIAA1189 (Accession XM\_050508). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1189. Phospholipase A2-activating Protein (PLAA, Accession NM\_004253) is another VGAM1662 host target gene. PLAA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of PLAA BINDING SITE, designated SEQ ID:10441, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56189] Another function of VGAM1662 is therefore inhibition of Phospholipase A2-activating Protein (PLAA, Accession NM\_004253). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAA. Solute Carrier Family 2 (facilitated glucose transporter), Member 13 (SLC2A13, Accession NM\_052885) is another VGAM1662 host target gene. SLC2A13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A13 BINDING SITE, designated SEQ ID:27466, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56190] Another function of VGAM1662 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter), Member 13 (SLC2A13, Accession NM\_052885). Accordingly, utilities of VGAM1662 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with SLC2A13. Extracellular Link Domain Containing 1 (XLKD1, Accession NM\_006691) is another VGAM1662 host target gene. XLKD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XLKD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XLKD1 BINDING SITE, designated SEQ ID:13507, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56191] Another function of VGAM1662 is therefore inhibition of Extracellular Link Domain Containing 1 (XLKD1, Accession NM\_006691). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XLKD1. LOC144997 (Accession XM\_096702) is another VGAM1662 host target gene. LOC144997 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144997, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC144997 BINDING SITE, designated SEQ ID:40483, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56192] Another function of VGAM1662 is therefore inhibition of LOC144997 (Accession XM\_096702). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144997. LOC149076 (Accession XM\_086415) is another VGAM1662 host target gene. LOC149076 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149076, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149076 BINDING SITE, designated SEQ ID:38638, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56193] Another function of VGAM1662 is therefore inhibition of LOC149076 (Accession XM\_086415). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149076. LOC152674 (Accession XM\_098251) is an-

other VGAM1662 host target gene. LOC152674 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152674, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152674 BINDING SITE, designated SEQ ID:41538, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56194] Another function of VGAM1662 is therefore inhibition of LOC152674 (Accession XM\_098251). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152674. LOC158038 (Accession XM\_088446) is another VGAM1662 host target gene. LOC158038 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158038 BINDING SITE, designated SEQ ID:39700, to the nucleotide sequence of VGAM1662 RNA, herein designated VGAM RNA, also designated SEQ ID:4373.

[56195] Another function of VGAM1662 is therefore inhibition of LOC158038 (Accession XM\_088446). Accordingly, utilities of VGAM1662 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158038. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1663 (VGAM1663) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56196] VGAM1663 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1663 was detected is described hereinabove with reference to Figs. 1–8.

[56197] VGAM1663 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1663 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56198] VGAM1663 gene encodes a VGAM1663 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1663 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1663 precursor RNA is designated SEQ ID:1649, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1649 is located at position 98907 relative to the genome of Cercopithecine Herpesvirus 7.

[56199] VGAM1663 precursor RNA folds onto itself, forming VGAM1663 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56200] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1663 folded precursor RNA into VGAM1663 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other



necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1663 RNA is designated SEQ ID:4374, and is provided hereinbelow with reference to the sequence listing part.

[56201] VGAM1663 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1663 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1663 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56202] VGAM1663 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1663 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1663 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1663 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1663 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56203] The complementary binding of VGAM1663 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1663 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1663 host target RNA into VGAM1663 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56204] It is appreciated that VGAM1663 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1663 host target genes. The mRNA of each one of this plurality of VGAM1663 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1663 RNA, herein designated VGAM RNA, and which when bound by VGAM1663 RNA causes inhibition of translation of respective one or more VGAM1663 host target proteins.

[56205] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1663 gene, herein designated VGAM GENE, on one or more VGAM1663 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56206] It is yet further appreciated that a function of VGAM1663 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1663 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1663 correlate with, and may be deduced from, the identity of the host target genes which VGAM1663 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56207] Nucleotide sequences of the VGAM1663 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1663 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1663 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1663 are further described hereinbelow with reference to Table 1.

[56208] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1663 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1663 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[56209] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1663 gene, herein designated VGAM is inhibition of expression of VGAM1663 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1663 correlate with, and may be deduced from, the identity of the target genes which VGAM1663 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56210] EphA3 (EPHA3, Accession NM\_005233) is a VGAM1663 host target gene. EPHA3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EPHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA3 BINDING SITE, designated SEQ ID:11741, to the nucleotide sequence of VGAM1663 RNA, herein designated VGAM RNA, also designated SEQ ID:4374.

[56211] A function of VGAM1663 is therefore inhibition of EphA3 (EPHA3, Accession NM\_005233), a gene which binds to ephrin-a2, -a3, -a4 and -a5. could play a role in lymphoid function. Accordingly, utilities of VGAM1663 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA3. The function of EPHA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM164. Natriuretic Peptide Receptor A/guanylate Cyclase A (atrionatriuretic peptide receptor A) (NPR1, Accession XM\_113360) is another VGAM1663 host target gene. NPR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NPR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPR1 BINDING SITE, designated SEQ ID:42234, to the nucleotide sequence of VGAM1663 RNA, herein designated VGAM RNA, also designated SEQ ID:4374.

[56212] Another function of VGAM1663 is therefore inhibition of Natriuretic Peptide Receptor A/guanylate Cyclase A (atrionatriuretic peptide receptor A) (NPR1, Accession XM\_113360), a gene which has guanylate cyclase activity on binding of anp. Accordingly, utilities of VGAM1663 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPR1. The function of

NPR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM719.SH3-domain Binding Protein 2 (SH3BP2, Accession NM\_003023) is another VGAM1663 host target gene. SH3BP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP2 BINDING SITE, designated SEQ ID:8943, to the nucleotide sequence of VGAM1663 RNA, herein designated VGAM RNA, also designated SEQ ID:4374.

[56213] Another function of VGAM1663 is therefore inhibition of SH3-domain Binding Protein 2 (SH3BP2, Accession NM\_003023). Accordingly, utilities of VGAM1663 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BP2. CDC14 Cell Division Cycle 14 Homolog A (*S. cerevisiae*) (CDC14A, Accession NM\_003672) is another VGAM1663 host target gene. CDC14A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

CDC14A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14A BINDING SITE, designated SEQ ID:9763, to the nucleotide sequence of VGAM1663 RNA, herein designated VGAM RNA, also designated SEQ ID:4374.

[56214] Another function of VGAM1663 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog A (*S. cerevisiae*) (CDC14A, Accession NM\_003672). Accordingly, utilities of VGAM1663 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14A. LOC219376 (Accession XM\_168147) is another VGAM1663 host target gene. LOC219376 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219376, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219376 BINDING SITE, designated SEQ ID:45068, to the nucleotide sequence of VGAM1663 RNA, herein designated VGAM RNA, also designated SEQ ID:4374.

[56215] Another function of VGAM1663 is therefore inhibition of



LOC219376 (Accession XM\_168147). Accordingly, utilities of VGAM1663 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219376. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1664 (VGAM1664) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56216] VGAM1664 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1664 was detected is described hereinabove with reference to Figs. 1-8.

[56217] VGAM1664 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1664 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56218] VGAM1664 gene encodes a VGAM1664 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1664 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1664 precursor RNA is designated SEQ ID:1650, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1650 is located at position 105330 relative to the genome of Cercopithecine Herpesvirus 7.

- [56219] VGAM1664 precursor RNA folds onto itself, forming VGAM1664 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [56220] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1664 folded precursor RNA into VGAM1664 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide se-

quence of VGAM1664 RNA is designated SEQ ID:4375, and is provided hereinbelow with reference to the sequence listing part.

[56221] VGAM1664 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1664 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1664 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56222] VGAM1664 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1664 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1664 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1664 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1664 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[56223] The complementary binding of VGAM1664 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1664 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1664 host target RNA into VGAM1664 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56224] It is appreciated that VGAM1664 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1664 host target genes. The mRNA of each one of this plurality of VGAM1664 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1664 RNA, herein designated VGAM RNA, and which when bound by VGAM1664 RNA causes inhibition of translation of respective one or more VGAM1664 host target proteins.

[56225] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1664 gene, herein designated VGAM GENE, on one or more VGAM1664 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56226] It is yet further appreciated that a function of VGAM1664

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1664 correlate with, and may be deduced from, the identity of the host target genes which VGAM1664 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56227] Nucleotide sequences of the VGAM1664 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1664 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1664 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1664 are further described hereinbelow with reference to Table 1.

[56228] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1664 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1664 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56229] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1664 gene, herein designated VGAM is inhibition of expression of VGAM1664 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1664 correlate with, and may be deduced from, the identity of the target genes which VGAM1664 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56230] BLAME (Accession NM\_020125) is a VGAM1664 host target gene. BLAME BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BLAME, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLAME BINDING SITE, designated SEQ ID:21307, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56231] A function of VGAM1664 is therefore inhibition of BLAME (Accession NM\_020125). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLAME. DXYS155E (Accession NM\_005088) is another VGAM1664

host target gene. DXYS155E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DXYS155E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DXYS155E BINDING SITE, designated SEQ ID:11543, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56232] Another function of VGAM1664 is therefore inhibition of DXYS155E (Accession NM\_005088), a gene which may be involved in b-cell activation. may also be involved in signal transduction and gene regulation. Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DXYS155E. The function of DXYS155E and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM766. Engrailed Homolog 1 (EN1, Accession NM\_001426) is another VGAM1664 host target gene. EN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EN1, corresponding to a HOST TARGET binding site such



as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EN1 BINDING SITE, designated SEQ ID:7140, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56233] Another function of VGAM1664 is therefore inhibition of Engrailed Homolog 1 (EN1, Accession NM\_001426), a gene which is a member of the homeodomain family of DNA binding proteins; may regulate gene expression, morphogenesis, and differentiation;. Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EN1. The function of EN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1615. Sialyltransferase 8E (alpha-2, 8-polysialyltransferase) (SIAT8E, Accession XM\_008705) is another VGAM1664 host target gene. SIAT8E BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SIAT8E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT8E BIND-

ING SITE, designated SEQ ID:30090, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56234] Another function of VGAM1664 is therefore inhibition of Sialyltransferase 8E (alpha-2, 8-polysialyltransferase) (SIAT8E, Accession XM\_008705). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT8E. Tumor Necrosis Factor Receptor Superfamily, Member 6b, Decoy (TNFRSF6B, Accession NM\_032945) is another VGAM1664 host target gene. TNFRSF6B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TNFRSF6B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF6B BINDING SITE, designated SEQ ID:26762, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56235] Another function of VGAM1664 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 6b, Decoy (TNFRSF6B, Accession NM\_032945), a gene which is decoy receptor and protects against apoptosis. Accord-

ingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF6B. The function of TNFRSF6B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM610.FLJ22246 (Accession NM\_025232) is another VGAM1664 host target gene. FLJ22246 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22246, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22246 BINDING SITE, designated SEQ ID:24910, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56236] Another function of VGAM1664 is therefore inhibition of FLJ22246 (Accession NM\_025232). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22246. KIAA1091 (Accession XM\_045750) is another VGAM1664 host target gene. KIAA1091 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by KIAA1091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1091 BINDING SITE, designated SEQ ID:34542, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56237] Another function of VGAM1664 is therefore inhibition of KIAA1091 (Accession XM\_045750). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1091. KIAA1691 (Accession XM\_166523) is another VGAM1664 host target gene. KIAA1691 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1691, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1691 BINDING SITE, designated SEQ ID:44466, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56238] Another function of VGAM1664 is therefore inhibition of KIAA1691 (Accession XM\_166523). Accordingly, utilities

of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1691. RAB39, Member RAS Oncogene Family (RAB39, Accession XM\_084662) is another VGAM1664 host target gene. RAB39 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB39 BINDING SITE, designated SEQ ID:37644, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56239] Another function of VGAM1664 is therefore inhibition of RAB39, Member RAS Oncogene Family (RAB39, Accession XM\_084662). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB39. LOC150407 (Accession XM\_086906) is another VGAM1664 host target gene. LOC150407 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150407 BINDING SITE, designated SEQ ID:38953, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56240] Another function of VGAM1664 is therefore inhibition of LOC150407 (Accession XM\_086906). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150407. LOC169026 (Accession XM\_095471) is another VGAM1664 host target gene. LOC169026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169026 BINDING SITE, designated SEQ ID:40264, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56241] Another function of VGAM1664 is therefore inhibition of LOC169026 (Accession XM\_095471). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC169026. LOC203392 (Accession XM\_114696) is another VGAM1664 host target gene. LOC203392 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203392, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203392 BINDING SITE, designated SEQ ID:43041, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56242] Another function of VGAM1664 is therefore inhibition of LOC203392 (Accession XM\_114696). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203392. LOC222166 (Accession XM\_168425) is another VGAM1664 host target gene. LOC222166 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222166 BINDING SITE, designated SEQ ID:45152, to the nucleotide sequence of VGAM1664 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4375.

[56243] Another function of VGAM1664 is therefore inhibition of LOC222166 (Accession XM\_168425). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222166. LOC93082 (Accession NM\_138397) is another VGAM1664 host target gene. LOC93082 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93082 BINDING SITE, designated SEQ ID:28766, to the nucleotide sequence of VGAM1664 RNA, herein designated VGAM RNA, also designated SEQ ID:4375.

[56244] Another function of VGAM1664 is therefore inhibition of LOC93082 (Accession NM\_138397). Accordingly, utilities of VGAM1664 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93082. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1665 (VGAM1665) viral gene, which



modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56245] VGAM1665 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1665 was detected is described hereinabove with reference to Figs. 1–8.

[56246] VGAM1665 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Spleen and Kidney Necrosis Virus. VGAM1665 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56247] VGAM1665 gene encodes a VGAM1665 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1665 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1665 precursor RNA is designated SEQ ID:1651, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1651 is located at position 60134 relative to the genome of Infectious Spleen and Kidney Necrosis Virus.

[56248] VGAM1665 precursor RNA folds onto itself, forming

VGAM1665 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56249] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1665 folded precursor RNA into VGAM1665 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1665 RNA is designated SEQ ID:4376, and is provided hereinbelow with reference to the sequence listing part.

[56250] VGAM1665 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1665 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1665 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56251] VGAM1665 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1665 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1665 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1665 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1665 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56252] The complementary binding of VGAM1665 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1665 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1665 host target RNA into VGAM1665 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56253] It is appreciated that VGAM1665 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1665 host target genes. The mRNA of each one of this plurality of VGAM1665 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1665 RNA, herein designated VGAM RNA, and which when bound by VGAM1665 RNA causes inhibition of translation of respective one or more VGAM1665 host target proteins.

[56254] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1665 gene, herein designated VGAM GENE, on one or more VGAM1665 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56255] It is yet further appreciated that a function of VGAM1665 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1665 include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1665 correlate with, and may be deduced from, the identity of the host target genes which

VGAM1665 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56256] Nucleotide sequences of the VGAM1665 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1665 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1665 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1665 are further described hereinbelow with reference to Table 1.

[56257] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1665 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1665 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56258] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1665 gene, herein designated VGAM is inhibition of expression of VGAM1665 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1665 correlate with, and may be deduced from, the identity of the target genes which VGAM1665 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[56259] Trichorhinophalangeal Syndrome I (TRPS1, Accession NM\_014112) is a VGAM1665 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15348, to the nucleotide sequence of VGAM1665 RNA, herein designated VGAM RNA, also designated SEQ ID:4376.

[56260] A function of VGAM1665 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM\_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM1665 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172.E2IG4 (Accession XM\_165623) is another VGAM1665 host target gene. E2IG4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by E2IG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of E2IG4 BINDING SITE, designated SEQ ID:43702, to the nucleotide sequence of VGAM1665 RNA, herein designated VGAM RNA, also designated SEQ ID:4376.

[56261] Another function of VGAM1665 is therefore inhibition of E2IG4 (Accession XM\_165623). Accordingly, utilities of VGAM1665 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E2IG4. FLJ13710 (Accession NM\_024817) is another VGAM1665 host target gene. FLJ13710 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13710, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13710 BINDING SITE, designated SEQ ID:24204, to the nucleotide sequence of VGAM1665 RNA, herein designated VGAM RNA, also designated SEQ ID:4376.

[56262] Another function of VGAM1665 is therefore inhibition of FLJ13710 (Accession NM\_024817). Accordingly, utilities of



VGAM1665 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13710. KIAA1582 (Accession XM\_037262) is another VGAM1665 host target gene. KIAA1582 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1582, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1582 BINDING SITE, designated SEQ ID:32586, to the nucleotide sequence of VGAM1665 RNA, herein designated VGAM RNA, also designated SEQ ID:4376.

[56263] Another function of VGAM1665 is therefore inhibition of KIAA1582 (Accession XM\_037262). Accordingly, utilities of VGAM1665 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1582. KIAA1706 (Accession XM\_166595) is another VGAM1665 host target gene. KIAA1706 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1706 BINDING SITE, designated SEQ ID:44576, to the nucleotide sequence of VGAM1665 RNA, herein designated VGAM RNA, also designated SEQ ID:4376.

[56264] Another function of VGAM1665 is therefore inhibition of KIAA1706 (Accession XM\_166595). Accordingly, utilities of VGAM1665 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1706. Purinergic Receptor P2X-like 1, Orphan Receptor (P2RXL1, Accession NM\_005446) is another VGAM1665 host target gene. P2RXL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P2RXL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RXL1 BINDING SITE, designated SEQ ID:11928, to the nucleotide sequence of VGAM1665 RNA, herein designated VGAM RNA, also designated SEQ ID:4376.

[56265] Another function of VGAM1665 is therefore inhibition of Purinergic Receptor P2X-like 1, Orphan Receptor (P2RXL1, Accession NM\_005446). Accordingly, utilities of VGAM1665 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

P2RXL1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1666 (VGAM1666) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56266] VGAM1666 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1666 was detected is described hereinabove with reference to Figs. 1–8.

[56267] VGAM1666 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Spleen and Kidney Necrosis Virus. VGAM1666 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56268] VGAM1666 gene encodes a VGAM1666 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1666 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1666 precursor RNA is designated SEQ ID:1652, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1652 is located at position 58471 relative to the genome of Infectious Spleen and Kidney Necrosis Virus.

[56269] VGAM1666 precursor RNA folds onto itself, forming VGAM1666 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56270] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1666 folded precursor RNA into VGAM1666 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1666 RNA is designated SEQ ID:4377, and is provided hereinbelow with reference to the sequence listing part.

[56271] VGAM1666 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1666 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1666 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[56272] VGAM1666 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1666 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1666 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1666 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1666 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[56273] The complementary binding of VGAM1666 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1666 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1666 host target RNA into VGAM1666 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56274] It is appreciated that VGAM1666 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1666 host target genes. The mRNA of each one of this plurality of VGAM1666 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1666 RNA, herein designated VGAM RNA, and which when bound by VGAM1666 RNA causes

inhibition of translation of respective one or more VGAM1666 host target proteins.

[56275] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1666 gene, herein designated VGAM GENE, on one or more VGAM1666 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56276] It is yet further appreciated that a function of VGAM1666 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1666 include diagnosis, prevention and

treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1666 correlate with, and may be deduced from, the identity of the host target genes which VGAM1666 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56277] Nucleotide sequences of the VGAM1666 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1666 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1666 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1666 are further described hereinbelow with reference to Table 1.

[56278] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1666 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1666 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56279] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1666 gene, herein designated VGAM is inhibition of expression of VGAM1666 target genes. It is



appreciated that specific functions, and accordingly utilities, of VGAM1666 correlate with, and may be deduced from, the identity of the target genes which VGAM1666 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56280] Coagulation Factor VIII, Procoagulant Component (hemophilia A) (F8, Accession NM\_000132) is a VGAM1666 host target gene. F8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by F8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F8 BINDING SITE, designated SEQ ID:5615, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56281] A function of VGAM1666 is therefore inhibition of Coagulation Factor VIII, Procoagulant Component (hemophilia A) (F8, Accession NM\_000132). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F8. Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM\_085943) is another VGAM1666 host target

gene. GRLF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRLF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRLF1 BINDING SITE, designated SEQ ID:38411, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56282] Another function of VGAM1666 is therefore inhibition of Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM\_085943), a gene which inhibits transcription of the glucocorticoid receptor gene. Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRLF1. The function of GRLF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. IRTA1 (Accession NM\_031282) is another VGAM1666 host target gene. IRTA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRTA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRTA1 BINDING SITE, designated SEQ ID:25302, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56283] Another function of VGAM1666 is therefore inhibition of IRTA1 (Accession NM\_031282). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRTA1. PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM\_012231) is another VGAM1666 host target gene. PRDM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRDM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM2 BINDING SITE, designated SEQ ID:14533, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56284] Another function of VGAM1666 is therefore inhibition of PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM\_012231), a gene which plays a role in tran-

scriptional regulation during neuronal differentiation and pathogenesis of retinoblastoma. Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM2. The function of PRDM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. TEM6 (Accession NM\_022748) is another VGAM1666 host target gene. TEM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM6 BINDING SITE, designated SEQ ID:22963, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56285] Another function of VGAM1666 is therefore inhibition of TEM6 (Accession NM\_022748), a gene which displays elevated expression during tumor angiogenesis. Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM6. The function of TEM6 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM175. Tripartite Motif-containing 34 (TRIM34, Accession NM\_130389) is another VGAM1666 host target gene. TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRIM34, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2, designated SEQ ID:28174 and SEQ ID:22250 respectively, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56286] Another function of VGAM1666 is therefore inhibition of Tripartite Motif-containing 34 (TRIM34, Accession NM\_130389). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM34. E2IG4 (Accession XM\_165623) is another VGAM1666 host target gene. E2IG4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by E2IG4, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of E2IG4 BINDING SITE, designated SEQ ID:43701, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56287] Another function of VGAM1666 is therefore inhibition of E2IG4 (Accession XM\_165623). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E2IG4. FLJ00001 (Accession XM\_088525) is another VGAM1666 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00001 BINDING SITE, designated SEQ ID:39782, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56288] Another function of VGAM1666 is therefore inhibition of FLJ00001 (Accession XM\_088525). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ00001. KIAA0513 (Accession NM\_014732) is another VGAM1666 host target gene. KIAA0513 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0513 BINDING SITE, designated SEQ ID:16353, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56289] Another function of VGAM1666 is therefore inhibition of KIAA0513 (Accession NM\_014732). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0513. KIAA1061 (Accession XM\_048786) is another VGAM1666 host target gene. KIAA1061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1061 BINDING SITE, designated SEQ ID:35269, to the nucleotide sequence of VGAM1666 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4377.

[56290] Another function of VGAM1666 is therefore inhibition of KIAA1061 (Accession XM\_048786). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1061. KIAA1297 (Accession XM\_051005) is another VGAM1666 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35715, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56291] Another function of VGAM1666 is therefore inhibition of KIAA1297 (Accession XM\_051005). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. KIAA1970 (Accession XM\_058808) is another VGAM1666 host target gene. KIAA1970 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1970, corresponding to



a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1970 BINDING SITE, designated SEQ ID:36753, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56292] Another function of VGAM1666 is therefore inhibition of KIAA1970 (Accession XM\_058808). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1970. Lectin, Galactoside-binding, Soluble, 8 (galectin 8) (LGALS8, Accession NM\_006499) is another VGAM1666 host target gene. LGALS8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LGALS8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGALS8 BINDING SITE, designated SEQ ID:13245, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56293] Another function of VGAM1666 is therefore inhibition of Lectin, Galactoside-binding, Soluble, 8 (galectin 8)

(LGALS8, Accession NM\_006499). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGALS8. MAC30 (Accession XM\_031536) is another VGAM1666 host target gene. MAC30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAC30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAC30 BINDING SITE, designated SEQ ID:31403, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56294] Another function of VGAM1666 is therefore inhibition of MAC30 (Accession XM\_031536). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAC30. MGC1136 (Accession NM\_024025) is another VGAM1666 host target gene. MGC1136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC1136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of MGC1136 BINDING SITE, designated SEQ ID:23454, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56295] Another function of VGAM1666 is therefore inhibition of MGC1136 (Accession NM\_024025). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC1136. MGC12945 (Accession NM\_032318) is another VGAM1666 host target gene. MGC12945 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC12945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12945 BINDING SITE, designated SEQ ID:26118, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56296] Another function of VGAM1666 is therefore inhibition of MGC12945 (Accession NM\_032318). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12945. Sialyltransferase 8C

(alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase) (SIAT8C, Accession NM\_015879) is another VGAM1666 host target gene. SIAT8C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SIAT8C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT8C BINDING SITE, designated SEQ ID:18024, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56297] Another function of VGAM1666 is therefore inhibition of Sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase) (SIAT8C, Accession NM\_015879). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT8C. T-cell Leukemia/lymphoma 6 (TCL6, Accession NM\_020552) is another VGAM1666 host target gene. TCL6 BINDING SITE1 through TCL6 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCL6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of TCL6 BINDING SITE1 through TCL6 BINDING SITE4, designated SEQ ID:21765, SEQ ID:21757, SEQ ID:15763 and SEQ ID:14840 respectively, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56298] Another function of VGAM1666 is therefore inhibition of T-cell Leukemia/lymphoma 6 (TCL6, Accession NM\_020552). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCL6. LOC199990 (Accession XM\_114083) is another VGAM1666 host target gene. LOC199990 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199990, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199990 BINDING SITE, designated SEQ ID:42684, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56299] Another function of VGAM1666 is therefore inhibition of LOC199990 (Accession XM\_114083). Accordingly, utilities

of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199990. LOC201229 (Accession XM\_113925) is another VGAM1666 host target gene. LOC201229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201229 BINDING SITE, designated SEQ ID:42544, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56300] Another function of VGAM1666 is therefore inhibition of LOC201229 (Accession XM\_113925). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201229. LOC86651 (Accession XM\_044052) is another VGAM1666 host target gene. LOC86651 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC86651, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC86651 BINDING SITE, designated SEQ ID:34095, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56301] Another function of VGAM1666 is therefore inhibition of LOC86651 (Accession XM\_044052). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC86651. LOC90378 (Accession XM\_031299) is another VGAM1666 host target gene. LOC90378 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90378, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90378 BINDING SITE, designated SEQ ID:31335, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56302] Another function of VGAM1666 is therefore inhibition of LOC90378 (Accession XM\_031299). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90378. LOC91694 (Accession XM\_040082) is another VGAM1666 host target gene. LOC91694 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91694 BINDING SITE, designated SEQ ID:33248, to the nucleotide sequence of VGAM1666 RNA, herein designated VGAM RNA, also designated SEQ ID:4377.

[56303] Another function of VGAM1666 is therefore inhibition of LOC91694 (Accession XM\_040082). Accordingly, utilities of VGAM1666 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91694. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1667 (VGAM1667) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56304] VGAM1667 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1667 was detected is described hereinabove with reference to Figs. 1-8.



[56305] VGAM1667 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Spleen and Kidney Necrosis Virus. VGAM1667 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56306] VGAM1667 gene encodes a VGAM1667 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1667 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1667 precursor RNA is designated SEQ ID:1653, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1653 is located at position 52329 relative to the genome of Infectious Spleen and Kidney Necrosis Virus.

[56307] VGAM1667 precursor RNA folds onto itself, forming VGAM1667 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[56308] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1667 folded precursor RNA into VGAM1667 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1667 RNA is designated SEQ ID:4378, and is provided hereinbelow with reference to the sequence listing part.

[56309] VGAM1667 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1667 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1667 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56310] VGAM1667 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1667 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1667 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1667 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1667 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56311] The complementary binding of VGAM1667 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1667 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1667 host target RNA into VGAM1667 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56312] It is appreciated that VGAM1667 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1667 host target genes. The mRNA of each one of this plurality of VGAM1667 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1667 RNA, herein designated VGAM RNA, and which when bound by VGAM1667 RNA causes inhibition of translation of respective one or more VGAM1667 host target proteins.

[56313] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1667 gene, herein designated VGAM GENE, on one or more VGAM1667 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56314] It is yet further appreciated that a function of VGAM1667 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1667 include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1667 correlate with, and may be deduced from, the identity of the host target genes which VGAM1667 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56315] Nucleotide sequences of the VGAM1667 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1667 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1667 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1667 are further described hereinbelow with reference to Table 1.

[56316] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1667 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1667 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56317] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1667 gene, herein designated VGAM is inhibition of expression of VGAM1667 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1667 correlate with, and may be deduced from, the identity of the target genes which VGAM1667 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56318] Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM\_101395) is a VGAM1667 host target gene. DYRK1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DYRK1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE, designated SEQ ID:28162, to the nucleotide sequence of VGAM1667 RNA, herein designated VGAM RNA, also designated SEQ ID:4378.

[56319] A function of VGAM1667 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM\_101395), a gene which regulates cell proliferation and may be involved in brain development . Accordingly, utilities of VGAM1667 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK1A. The function of DYRK1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42.Cat Eye Syndrome Chromosome Region, Candidate 7 (CECR7, Accession XM\_086803) is another VGAM1667 host target gene. CECR7 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CECR7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CECR7 BINDING SITE,

designated SEQ ID:38877, to the nucleotide sequence of VGAM1667 RNA, herein designated VGAM RNA, also designated SEQ ID:4378.

[56320] Another function of VGAM1667 is therefore inhibition of Cat Eye Syndrome Chromosome Region, Candidate 7 (CECR7, Accession XM\_086803). Accordingly, utilities of VGAM1667 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR7. FLJ30058 (Accession NM\_144967) is another VGAM1667 host target gene. FLJ30058 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30058, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30058 BINDING SITE, designated SEQ ID:29582, to the nucleotide sequence of VGAM1667 RNA, herein designated VGAM RNA, also designated SEQ ID:4378.

[56321] Another function of VGAM1667 is therefore inhibition of FLJ30058 (Accession NM\_144967). Accordingly, utilities of VGAM1667 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30058. LOC146138 (Accession XM\_096938) is another



VGAM1667 host target gene. LOC146138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146138 BINDING SITE, designated SEQ ID:40654, to the nucleotide sequence of VGAM1667 RNA, herein designated VGAM RNA, also designated SEQ ID:4378.

[56322] Another function of VGAM1667 is therefore inhibition of LOC146138 (Accession XM\_096938). Accordingly, utilities of VGAM1667 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146138. LOC146443 (Accession XM\_085461) is another VGAM1667 host target gene. LOC146443 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146443 BINDING SITE, designated SEQ ID:38148, to the nucleotide sequence of VGAM1667 RNA, herein designated VGAM RNA, also designated SEQ ID:4378.

[56323] Another function of VGAM1667 is therefore inhibition of LOC146443 (Accession XM\_085461). Accordingly, utilities of VGAM1667 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146443. LOC221922 (Accession XM\_166555) is another VGAM1667 host target gene. LOC221922 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221922 BINDING SITE, designated SEQ ID:44531, to the nucleotide sequence of VGAM1667 RNA, herein designated VGAM RNA, also designated SEQ ID:4378.

[56324] Another function of VGAM1667 is therefore inhibition of LOC221922 (Accession XM\_166555). Accordingly, utilities of VGAM1667 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221922. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1668 (VGAM1668) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[56325] VGAM1668 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1668 was detected is described hereinabove with reference to Figs. 1–8.

[56326] VGAM1668 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1668 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56327] VGAM1668 gene encodes a VGAM1668 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1668 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1668 precursor RNA is designated SEQ ID:1654, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1654 is located at position 20850 relative to the genome of Human Adenovirus D.

[56328] VGAM1668 precursor RNA folds onto itself, forming VGAM1668 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56329] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1668 folded precursor RNA into VGAM1668 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1668 RNA is designated SEQ ID:4379, and is provided hereinbelow with reference to the sequence listing part.

[56330] VGAM1668 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1668 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1668 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56331] VGAM1668 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1668 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1668 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1668 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1668 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56332] The complementary binding of VGAM1668 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1668 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1668 host target RNA into VGAM1668 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56333] It is appreciated that VGAM1668 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1668 host target genes. The mRNA of each one of this plurality of VGAM1668 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1668 RNA, herein designated VGAM RNA, and which when bound by VGAM1668 RNA causes inhibition of translation of respective one or more VGAM1668 host target proteins.

[56334] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1668 gene, herein designated VGAM GENE, on one or more VGAM1668 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56335] It is yet further appreciated that a function of VGAM1668 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1668 correlate with, and may be deduced from, the identity of the host target genes which VGAM1668 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[56336] Nucleotide sequences of the VGAM1668 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1668 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1668 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1668 are further described hereinbelow with reference to Table 1.

[56337] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1668 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1668 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56338] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1668 gene, herein designated VGAM is inhibition of expression of VGAM1668 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1668 correlate with, and may be deduced from, the identity of the target genes which VGAM1668 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.



[56339] AXL Receptor Tyrosine Kinase (AXL, Accession NM\_001699) is a VGAM1668 host target gene. AXL BINDING SITE1 and AXL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AXL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AXL BINDING SITE1 and AXL BINDING SITE2, designated SEQ ID:7422 and SEQ ID:22443 respectively, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56340] A function of VGAM1668 is therefore inhibition of AXL Receptor Tyrosine Kinase (AXL, Accession NM\_001699). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AXL. Frizzled Homolog 4 (Drosophila) (FZD4, Accession NM\_012193) is another VGAM1668 host target gene. FZD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FZD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD4 BINDING SITE, designated SEQ

ID:14483, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56341] Another function of VGAM1668 is therefore inhibition of Frizzled Homolog 4 (Drosophila) (FZD4, Accession NM\_012193), a gene which may function in cell polarity, cell fate specification and cancer; similar to frizzled receptor family, has seven transmembrane domains. Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD4. The function of FZD4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM309.Glucose-6-phosphatase, Transport (glucose-6-phosphate) Protein 1 (G6PT1, Accession NM\_001467) is another VGAM1668 host target gene. G6PT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by G6PT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G6PT1 BINDING SITE, designated SEQ ID:7199,

to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56342] Another function of VGAM1668 is therefore inhibition of Glucose-6-phosphatase, Transport (glucose-6-phosphate) Protein 1 (G6PT1, Accession NM\_001467). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G6PT1. Potassium Intermediate/small Conductance Calcium-activated Channel, Subfamily N, Member 4 (KCNN4, Accession NM\_002250) is another VGAM1668 host target gene. KCNN4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNN4 BINDING SITE, designated SEQ ID:8037, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56343] Another function of VGAM1668 is therefore inhibition of Potassium Intermediate/small Conductance Calcium-activated Channel, Subfamily N, Member 4 (KCNN4, Accession NM\_002250), a gene which forms a voltage-in-

dependent potassium channel that is activated by intracellular calcium. Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNN4. The function of KCNN4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM\_165540) is another VGAM1668 host target gene. MAT1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAT1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAT1A BINDING SITE, designated SEQ ID:43668, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56344] Another function of VGAM1668 is therefore inhibition of Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM\_165540). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAT1A. Neuroblastoma

RAS Viral (v-ras) Oncogene Homolog (NRAS, Accession NM\_002524) is another VGAM1668 host target gene. NRAS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRAS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRAS BINDING SITE, designated SEQ ID:8360, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56345] Another function of VGAM1668 is therefore inhibition of Neuroblastoma RAS Viral (v-ras) Oncogene Homolog (NRAS, Accession NM\_002524), a gene which ras proteins bind gdp/gtp and possess intrinsic gtpase activity. Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRAS. The function of NRAS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM351. Secreted Frizzled-related Protein 1 (SFRP1, Accession NM\_003012) is another VGAM1668 host target gene. SFRP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by SFRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRP1 BINDING SITE, designated SEQ ID:8929, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56346] Another function of VGAM1668 is therefore inhibition of Secreted Frizzled-related Protein 1 (SFRP1, Accession NM\_003012), a gene which is a receptor for wnt proteins that may have an anti-apoptotic function. Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRP1. The function of SFRP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM250.FLJ10101 (Accession NM\_024718) is another VGAM1668 host target gene. FLJ10101 BINDING SITE1 and FLJ10101 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10101, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of FLJ10101 BINDING SITE1 and FLJ10101 BINDING SITE2, designated SEQ ID:24045 and SEQ ID:24046 respectively, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56347] Another function of VGAM1668 is therefore inhibition of FLJ10101 (Accession NM\_024718). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10101. KIAA0285 (Accession NM\_014807) is another VGAM1668 host target gene. KIAA0285 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0285 BINDING SITE, designated SEQ ID:16752, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56348] Another function of VGAM1668 is therefore inhibition of KIAA0285 (Accession NM\_014807). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0285. KIAA0350 (Accession XM\_028332) is another VGAM1668 host target gene. KIAA0350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0350 BINDING SITE, designated SEQ ID:30665, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56349] Another function of VGAM1668 is therefore inhibition of KIAA0350 (Accession XM\_028332). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0350. KIAA0669 (Accession NM\_014779) is another VGAM1668 host target gene. KIAA0669 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0669 BINDING SITE, designated SEQ ID:16626, to the nucleotide sequence of VGAM1668 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4379.

[56350] Another function of VGAM1668 is therefore inhibition of KIAA0669 (Accession NM\_014779). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0669. KIAA0731 (Accession XM\_039975) is another VGAM1668 host target gene. KIAA0731 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0731, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0731 BINDING SITE, designated SEQ ID:33239, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56351] Another function of VGAM1668 is therefore inhibition of KIAA0731 (Accession XM\_039975). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0731. KIAA0872 (Accession NM\_014940) is another VGAM1668 host target gene. KIAA0872 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0872, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0872 BINDING SITE, designated SEQ ID:17245, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56352] Another function of VGAM1668 is therefore inhibition of KIAA0872 (Accession NM\_014940). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0872. KIAA1172 (Accession XM\_047889) is another VGAM1668 host target gene. KIAA1172 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1172 BINDING SITE, designated SEQ ID:35078, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56353] Another function of VGAM1668 is therefore inhibition of KIAA1172 (Accession XM\_047889). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1172. LOC116411 (Accession XM\_058095) is another VGAM1668 host target gene. LOC116411 BINDING SITE1 through LOC116411 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC116411, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116411 BINDING SITE1 through LOC116411 BINDING SITE3, designated SEQ ID:36566, SEQ ID:36567 and SEQ ID:36572 respectively, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56354] Another function of VGAM1668 is therefore inhibition of LOC116411 (Accession XM\_058095). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116411. LOC152762 (Accession XM\_087518) is another VGAM1668 host target gene. LOC152762 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152762, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC152762 BINDING SITE, designated SEQ ID:39305, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56355] Another function of VGAM1668 is therefore inhibition of LOC152762 (Accession XM\_087518). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152762. LOC200093 (Accession XM\_032184) is another VGAM1668 host target gene. LOC200093 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200093 BINDING SITE, designated SEQ ID:31598, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56356] Another function of VGAM1668 is therefore inhibition of LOC200093 (Accession XM\_032184). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200093. LOC221468 (Accession NM\_145316) is an-

other VGAM1668 host target gene. LOC221468 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221468 BINDING SITE, designated SEQ ID:29826, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56357] Another function of VGAM1668 is therefore inhibition of LOC221468 (Accession NM\_145316). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221468. LOC92697 (Accession XM\_046715) is another VGAM1668 host target gene. LOC92697 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92697, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92697 BINDING SITE, designated SEQ ID:34806, to the nucleotide sequence of VGAM1668 RNA, herein designated VGAM RNA, also designated SEQ ID:4379.

[56358] Another function of VGAM1668 is therefore inhibition of LOC92697 (Accession XM\_046715). Accordingly, utilities of VGAM1668 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92697. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1669 (VGAM1669) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56359] VGAM1669 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1669 was detected is described hereinabove with reference to Figs. 1–8.

[56360] VGAM1669 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1669 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56361] VGAM1669 gene encodes a VGAM1669 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1669 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1669 precursor RNA is designated SEQ ID:1655, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1655 is located at position 18504 relative to the genome of Human Adenovirus D.

[56362] VGAM1669 precursor RNA folds onto itself, forming VGAM1669 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56363] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1669 folded precursor RNA into VGAM1669 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1669 RNA is designated SEQ ID:4380, and is provided hereinbelow with reference to the sequence listing part.

[56364] VGAM1669 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1669 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1669 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56365] VGAM1669 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1669 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1669 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the



number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1669 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1669 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56366] The complementary binding of VGAM1669 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1669 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1669 host target RNA into VGAM1669 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56367] It is appreciated that VGAM1669 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1669 host target genes. The mRNA of each one of this plurality of VGAM1669 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1669 RNA, herein designated VGAM RNA, and which when bound by VGAM1669 RNA causes inhibition of translation of respective one or more VGAM1669 host target proteins.

[56368] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1669 gene, herein designated VGAM GENE, on one or more VGAM1669 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56369] It is yet further appreciated that a function of VGAM1669 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1669 correlate with, and may be deduced from, the identity of the host target genes which VGAM1669 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56370] Nucleotide sequences of the VGAM1669 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1669 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1669 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1669 are further described hereinbelow with reference to Table 1.

[56371] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1669 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1669 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[56372] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1669 gene, herein designated VGAM is inhibition of expression of VGAM1669 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1669 correlate with, and may be deduced from, the identity of the target genes which VGAM1669 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56373] Carnitine O-octanoyltransferase (CROT, Accession NM\_021151) is a VGAM1669 host target gene. CROT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CROT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CROT BINDING SITE, designated SEQ ID:22123, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56374] A function of VGAM1669 is therefore inhibition of Carnitine O-octanoyltransferase (CROT, Accession NM\_021151), a gene which CROT plays a crucial role in the beta-oxidation of branched-chain fatty acids includ-

ing pristanic acid. Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CROT. The function of CROT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM70. Eukaryotic Translation Initiation Factor 4E Binding Protein 2 (EIF4EBP2, Accession NM\_004096) is another VGAM1669 host target gene. EIF4EBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF4EBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4EBP2 BINDING SITE, designated SEQ ID:10300, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56375] Another function of VGAM1669 is therefore inhibition of Eukaryotic Translation Initiation Factor 4E Binding Protein 2 (EIF4EBP2, Accession NM\_004096), a gene which binds EIF4E and negatively regulates initiation of translation. Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with EIF4EBP2. The function of EIF4EBP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM501.G Protein-coupled Receptor 44 (GPR44, Accession NM\_004778) is another VGAM1669 host target gene. GPR44 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR44, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR44 BINDING SITE, designated SEQ ID:11173, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56376] Another function of VGAM1669 is therefore inhibition of G Protein-coupled Receptor 44 (GPR44, Accession NM\_004778), a gene which mediates signals to the interior of the cell via activation of heterotrimeric G proteins . Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR44. The function of GPR44 has been established by previous studies. By PCR amplification of human genomic DNA using degenerate oligonu-

cleotides corresponding to transmembrane domains 3 and 7 of the mouse delta-opioid receptor and somatostatin receptors, Marchese et al. (1999) isolated a partial cDNA for a novel G protein-coupled receptor, which they designated GPR44. They obtained a full-length clone by screening a lambda human genomic library. GPR44 encodes a 472-amino acid protein that is closely related to chemoattractant receptors. Northern blot analysis revealed a 3.5-kb GPR44 transcript primarily in thalamus, frontal cortex, pons, and hippocampus and at lower levels in hypothalamus and caudate/putamen. A 3.4-kb transcript was detected in fetal liver, leukocytes, and thymus. Prostaglandin D2 (PGD2; OMIM Ref. No. 176803) and other prostanoids are synthesized by the constitutive cyclooxygenase COX1 (PTGS1; 176805) and its inducible isoform, COX2 (PTGS2; 600262). PGD2, which is implicated in allergic disease, elicits its biologic function through interaction with the DP receptor (PTGDR; 604687). Hirai et al. (2001) showed that PGD2 produced by activated mast cells uses CRTH2 to induce intracellular calcium mobilization and chemotaxis in Th2 cells in a G-alpha(i) (GNAI1; 139310)-dependent manner. In addition, they found that CRTH2 rather than DP mediates

PGD2-dependent migration of blood eosinophils and basophils. Functional analysis indicated that PGD2 signaling through DP is coupled to G-alpha(s) (GNAS; 139320) and does not induce chemotaxis.

[56377] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56378] Hirai, H.; Tanaka, K.; Yoshie, O.; Ogawa, K.; Kenmotsu, K.; Takamori, Y.; Ichimasa, M.; Sugamura, K.; Nakamura, M.; Takano, S.; Nagata, K. : Prostaglandin D2 selectively induces chemotaxis in T helper type 2 cells, eosinophils, and basophils via seven-transmembrane receptor CRTH2. J. Exp. Med. 193: 255-261, 2001. ; and

[56379] Marchese, A.; Sawzdargo, M.; Nguyen, T.; Cheng, R.; Heng, H. H. Q.; Nowak, T.; Im, D-S.; Lynch, K. R.; George, S. R.; O'Dowd, B. F. : Discovery of three novel orphan G-protein-coupled r.

[56380] Further studies establishing the function and utilities of GPR44 are found in John Hopkins OMIM database record ID 604837, and in cited publications numbered 694 and 9159 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434O047 (Accession NM\_015594) is another VGAM1669 host target



gene. DKFZP434O047 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP434O047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434O047 BINDING SITE, designated SEQ ID:17868, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56381] Another function of VGAM1669 is therefore inhibition of DKFZP434O047 (Accession NM\_015594). Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434O047. FLJ20716 (Accession NM\_017938) is another VGAM1669 host target gene. FLJ20716 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20716, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20716 BINDING SITE, designated SEQ ID:19631, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56382] Another function of VGAM1669 is therefore inhibition of FLJ20716 (Accession NM\_017938). Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20716. Heterogeneous Nuclear Ribonucleoprotein A3 (HNRPA3, Accession NM\_005758) is another VGAM1669 host target gene. HNRPA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPA3 BINDING SITE, designated SEQ ID:12322, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56383] Another function of VGAM1669 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein A3 (HNRPA3, Accession NM\_005758). Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPA3. MAGE-E1 (Accession NM\_030801) is another VGAM1669 host target gene. MAGE-E1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by MAGE-E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAGE-E1 BINDING SITE, designated SEQ ID:25103, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56384] Another function of VGAM1669 is therefore inhibition of MAGE-E1 (Accession NM\_030801). Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAGE-E1. Mal, T-cell Differentiation Protein 2 (MAL2, Accession NM\_052886) is another VGAM1669 host target gene. MAL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAL2 BINDING SITE, designated SEQ ID:27469, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56385] Another function of VGAM1669 is therefore inhibition of Mal, T-cell Differentiation Protein 2 (MAL2, Accession

NM\_052886). Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAL2. MGC15563 (Accession NM\_032876) is another VGAM1669 host target gene. MGC15563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15563 BINDING SITE, designated SEQ ID:26699, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56386] Another function of VGAM1669 is therefore inhibition of MGC15563 (Accession NM\_032876). Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15563. LOC204823 (Accession XM\_115621) is another VGAM1669 host target gene. LOC204823 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC204823 BINDING SITE, designated SEQ ID:43102, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56387] Another function of VGAM1669 is therefore inhibition of LOC204823 (Accession XM\_115621). Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204823. LOC255654 (Accession XM\_173036) is another VGAM1669 host target gene. LOC255654 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255654, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255654 BINDING SITE, designated SEQ ID:46302, to the nucleotide sequence of VGAM1669 RNA, herein designated VGAM RNA, also designated SEQ ID:4380.

[56388] Another function of VGAM1669 is therefore inhibition of LOC255654 (Accession XM\_173036). Accordingly, utilities of VGAM1669 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255654. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1670 (VGAM1670) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56389] VGAM1670 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1670 was detected is described hereinabove with reference to Figs. 1–8.

[56390] VGAM1670 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1670 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56391] VGAM1670 gene encodes a VGAM1670 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1670 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1670 precursor RNA is designated SEQ ID:1656, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1656 is located at position 16692 relative to the genome of Human Adenovirus D.

[56392] VGAM1670 precursor RNA folds onto itself, forming VGAM1670 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56393] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1670 folded precursor RNA into VGAM1670 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1670 RNA is designated SEQ ID:4381, and is provided hereinbelow with reference to the sequence listing part.

[56394] VGAM1670 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1670 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1670 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56395] VGAM1670 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1670 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1670 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1670 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1670 host target RNA,



herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[56396] The complementary binding of VGAM1670 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1670 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1670 host target RNA into VGAM1670 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56397] It is appreciated that VGAM1670 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1670 host target genes. The mRNA of each one of this plurality of VGAM1670 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1670 RNA, herein designated VGAM RNA, and which when bound by VGAM1670 RNA causes inhibition of translation of respective one or more

VGAM1670 host target proteins.

[56398] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1670 gene, herein designated VGAM GENE, on one or more VGAM1670 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56399] It is yet further appreciated that a function of VGAM1670 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Spe-

cific functions, and accordingly utilities, of VGAM1670 correlate with, and may be deduced from, the identity of the host target genes which VGAM1670 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56400] Nucleotide sequences of the VGAM1670 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1670 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1670 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1670 are further described hereinbelow with reference to Table 1.

[56401] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1670 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1670 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56402] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1670 gene, herein designated VGAM is inhibition of expression of VGAM1670 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1670 correlate with, and may be deduced from, the identity of the target genes which VGAM1670 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56403] A Disintegrin and Metalloproteinase Domain 19 (meltrin beta) (ADAM19, Accession NM\_033274) is a VGAM1670 host target gene. ADAM19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAM19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM19 BINDING SITE, designated SEQ ID:27095, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56404] A function of VGAM1670 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 19 (meltrin beta) (ADAM19, Accession NM\_033274), a gene which participates in the proteolytic processing of beta-type neuregulin isoforms . Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM19. The function of ADAM19 and its association with various diseases and

clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM\_001282) is another VGAM1670 host target gene. AP2B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP2B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP2B1 BINDING SITE, designated SEQ ID:6953, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56405] Another function of VGAM1670 is therefore inhibition of Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM\_001282), a gene which links clathrin to receptors in coated vesicles. Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP2B1. The function of AP2B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1126. Bone Morphogenetic Protein

Receptor, Type II (serine/threonine kinase) (BMP2, Accession NM\_001204) is another VGAM1670 host target gene. BMP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BMP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMP2 BINDING SITE, designated SEQ ID:6869, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56406] Another function of VGAM1670 is therefore inhibition of Bone Morphogenetic Protein Receptor, Type II (serine/threonine kinase) (BMP2, Accession NM\_001204). Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMP2. Cytochrome P450, Subfamily IVF, Polypeptide 3 (leukotriene B4 omega hydroxylase) (CYP4F3, Accession NM\_000896) is another VGAM1670 host target gene. CYP4F3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP4F3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP4F3 BINDING SITE, designated SEQ ID:6592, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56407] Another function of VGAM1670 is therefore inhibition of Cytochrome P450, Subfamily IVF, Polypeptide 3 (leukotriene B4 omega hydroxylase) (CYP4F3, Accession NM\_000896), a gene which converts leukotriene B4 into the less active 20-hydroxy-leukotriene B4. Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP4F3. The function of CYP4F3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM186. Exostoses (multiple)-like 1 (EXTL1, Accession NM\_004455) is another VGAM1670 host target gene. EXTL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EXTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL1 BINDING SITE, des-

ignated SEQ ID:10752, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56408] Another function of VGAM1670 is therefore inhibition of Exostoses (multiple)-like 1 (EXTL1, Accession NM\_004455), a gene which probably contribute to the synthesis of heparan sulfate and heparin. Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL1. The function of EXTL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM806. Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM\_012275) is another VGAM1670 host target gene. IL1F5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1F5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1F5 BINDING SITE, designated SEQ ID:14598, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.



[56409] Another function of VGAM1670 is therefore inhibition of Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM\_012275), a gene which is a novel interleukin-1 receptor antagonist gene. Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F5. The function of IL1F5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM263. Oligophrenin 1 (OPHN1, Accession NM\_002547) is another VGAM1670 host target gene. OPHN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPHN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPHN1 BINDING SITE, designated SEQ ID:8402, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56410] Another function of VGAM1670 is therefore inhibition of Oligophrenin 1 (OPHN1, Accession NM\_002547). Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with OPHN1. Periaxin (PRX, Accession NM\_020956) is another VGAM1670 host target gene. PRX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRX BINDING SITE, designated SEQ ID:21934, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56411] Another function of VGAM1670 is therefore inhibition of Periaxin (PRX, Accession NM\_020956), a gene which seems to be required for maintenance of peripheral nerve myelin sheath. may have a role in axon-glial interactions, possibly by interacting with the cytoplasmic domains of integral membrane proteins such as myelin-associated glycoprotein in the periaxonal regions of the schwann cell plasma membrane. may have a role in the early phases of myelin deposition. Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRX. The function of PRX and its association with various diseases and clinical conditions, has been established by previous studies, as

described hereinabove with reference to VGAM476. Zinc Finger Protein 192 (ZNF192, Accession NM\_006298) is another VGAM1670 host target gene. ZNF192 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF192, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF192 BINDING SITE, designated SEQ ID:12990, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56412] Another function of VGAM1670 is therefore inhibition of Zinc Finger Protein 192 (ZNF192, Accession NM\_006298). Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF192. H-L(3)MBT (Accession NM\_015478) is another VGAM1670 host target gene. H-L(3)MBT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H-L(3)MBT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H-L(3)MBT BINDING SITE, designated SEQ

ID:17755, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56413] Another function of VGAM1670 is therefore inhibition of H-L(3)MBT (Accession NM\_015478). Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H-L(3)MBT. KIAA1456 (Accession XM\_040100) is another VGAM1670 host target gene. KIAA1456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1456 BINDING SITE, designated SEQ ID:33264, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56414] Another function of VGAM1670 is therefore inhibition of KIAA1456 (Accession XM\_040100). Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1456. SZF1 (Accession NM\_016089) is another VGAM1670 host target gene. SZF1 BINDING SITE is HOST

TARGET binding site found in the 5` untranslated region of mRNA encoded by SZF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SZF1 BINDING SITE, designated SEQ ID:18175, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56415] Another function of VGAM1670 is therefore inhibition of SZF1 (Accession NM\_016089). Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SZF1. LOC146243 (Accession XM\_096956) is another VGAM1670 host target gene. LOC146243 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC146243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146243 BINDING SITE, designated SEQ ID:40679, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56416] Another function of VGAM1670 is therefore inhibition of

LOC146243 (Accession XM\_096956). Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146243. LOC257117 (Accession XM\_171238) is another VGAM1670 host target gene. LOC257117 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257117 BINDING SITE, designated SEQ ID:46025, to the nucleotide sequence of VGAM1670 RNA, herein designated VGAM RNA, also designated SEQ ID:4381.

[56417] Another function of VGAM1670 is therefore inhibition of LOC257117 (Accession XM\_171238). Accordingly, utilities of VGAM1670 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257117. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1671 (VGAM1671) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[56418] VGAM1671 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1671 was detected is described hereinabove with reference to Figs. 1–8.

[56419] VGAM1671 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1671 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56420] VGAM1671 gene encodes a VGAM1671 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1671 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1671 precursor RNA is designated SEQ ID:1657, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1657 is located at position 13911 relative to the genome of Human Adenovirus D.

[56421] VGAM1671 precursor RNA folds onto itself, forming VGAM1671 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56422] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1671 folded precursor RNA into VGAM1671 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1671 RNA is designated SEQ ID:4382, and is provided hereinbelow with reference to the sequence listing part.

[56423] VGAM1671 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1671 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1671 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-



ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[56424] VGAM1671 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1671 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1671 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1671 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1671 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[56425] The complementary binding of VGAM1671 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1671 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1671 host target RNA into VGAM1671 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56426] It is appreciated that VGAM1671 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1671 host target genes. The mRNA of each one of this plurality of VGAM1671 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1671 RNA, herein designated VGAM RNA, and which when bound by VGAM1671 RNA causes inhibition of translation of respective one or more VGAM1671 host target proteins.

[56427] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1671 gene, herein designated VGAM GENE, on one

or more VGAM1671 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56428] It is yet further appreciated that a function of VGAM1671 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1671 correlate with, and may be deduced from, the identity of the host target genes which VGAM1671 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56429] Nucleotide sequences of the VGAM1671 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1671 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1671 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1671 are further described hereinbelow with reference to Table 1.

[56430] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1671 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1671 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56431] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1671 gene, herein designated VGAM is inhibition of expression of VGAM1671 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1671 correlate with, and may be deduced from, the identity of the target genes which VGAM1671 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56432] CRACC (Accession NM\_021181) is a VGAM1671 host tar-

get gene. CRACC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRACC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRACC BINDING SITE, designated SEQ ID:22157, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56433] A function of VGAM1671 is therefore inhibition of CRACC (Accession NM\_021181), a gene which may participate in adhesion reactions between T lymphocytes and accessory cells. Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRACC. The function of CRACC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM26.DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 11 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX11, Accession NM\_030655) is another VGAM1671 host target gene. DDX11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

DDX11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX11 BINDING SITE, designated SEQ ID:24987, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56434] Another function of VGAM1671 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 11 (CHL1–like helicase homolog, *S. cerevisiae*) (DDX11, Accession NM\_030655), a gene which could be an ATP–dependent DNA–binding helicase and may intervene in cell cycle regulation. Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX11. The function of DDX11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1533.24–dehydrocholesterol Reductase (DHCR24, Accession NM\_014762) is another VGAM1671 host target gene. DHCR24 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DHCR24, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DHCR24 BINDING SITE, designated SEQ ID:16524, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56435] Another function of VGAM1671 is therefore inhibition of 24-dehydrocholesterol Reductase (DHCR24, Accession NM\_014762), a gene which catalyzes the reduction of sterol intermediates. Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DHCR24. The function of DHCR24 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM235. Dystrophia Myotonica-protein Kinase (DMPK, Accession NM\_004409) is another VGAM1671 host target gene. DMPK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DMPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMPK BINDING SITE, designated SEQ ID:10668,

to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56436] Another function of VGAM1671 is therefore inhibition of Dystrophia Myotonica-protein Kinase (DMPK, Accession NM\_004409). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMPK. Dual Specificity Phosphatase 4 (DUSP4, Accession NM\_057158) is another VGAM1671 host target gene. DUSP4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DUSP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP4 BINDING SITE, designated SEQ ID:27668, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56437] Another function of VGAM1671 is therefore inhibition of Dual Specificity Phosphatase 4 (DUSP4, Accession NM\_057158), a gene which regulates mitogenic signal transduction. Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DUSP4. The function of



DUSP4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM110.GASC1 (Accession XM\_034624) is another VGAM1671 host target gene. GASC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GASC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GASC1 BINDING SITE, designated SEQ ID:32125, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56438] Another function of VGAM1671 is therefore inhibition of GASC1 (Accession XM\_034624), a gene which may play an important role in the development and/or progression of various types of cancer . Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GASC1. The function of GASC1 has been established by previous studies. Frequent amplification of DNA copy number at chromosome 9p24-p23 has been demonstrated in cell lines derived from esophageal squamous cell carcinomas

(Yang et al., 2000). Yang et al. (2000) used fluorescence in situ hybridization and Southern blot analysis to map the 9p24–p23 amplicon. They then screened target genes/transcripts present within this amplicon by Northern blot analysis. With this strategy, they cloned a novel gene, which they designated 'gene amplified in squamous cell carcinoma–1' (GASC1), that was amplified and overexpressed in several cell lines. The deduced 1,056–amino acid GASC1 protein contains 2 PHD finger motifs and a PX domain. PHD finger motifs are zinc finger–like sequences found in nuclear proteins that participate in chromatin–mediated transcriptional regulation and are present in a number of protooncogenes. Yang et al. (2000) suggested that overexpression of GASC1 may play an important role in the development and/or progression of various types of cancer, including esophageal squamous cell carcinoma. Nagase et al. (1998) mapped the GASC1 gene, which they designated KIAA0780, to chromosome 9 by radiation hybrid analysis.

[56439] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56440] Nagase, T.; Ishikawa, K.; Suyama, M.; Kikuno, R.; Miyajima,

N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. XI. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro. DNA Res. 5: 277–286, 1998. ; and

[56441] Yang, Z.-Q.; Imoto, I.; Fukuda, Y.; Pimkhaokham, A.; Shimada, Y.; Imamura, M.; Sugano, S.; Nakamura, Y.; Inazawa, J. : Identification of a novel gene, GASC1, within an amplicon at 9p23-.

[56442] Further studies establishing the function and utilities of GASC1 are found in John Hopkins OMIM database record ID 605469, and in cited publications numbered 7048 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LIM Domain Only 2 (rhombotin-like 1) (LMO2, Accession NM\_005574) is another VGAM1671 host target gene. LMO2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LMO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMO2 BINDING SITE, designated SEQ ID:12100, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA,

also designated SEQ ID:4382.

[56443] Another function of VGAM1671 is therefore inhibition of LIM Domain Only 2 (rhombotin-like 1) (LMO2, Accession NM\_005574). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMO2. Leucine-zipper-like Transcriptional Regulator, 1 (LZTR1, Accession NM\_006767) is another VGAM1671 host target gene. LZTR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LZTR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTR1 BINDING SITE, designated SEQ ID:13641, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56444] Another function of VGAM1671 is therefore inhibition of Leucine-zipper-like Transcriptional Regulator, 1 (LZTR1, Accession NM\_006767). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTR1. Mucin 4, Tracheobronchial (MUC4, Accession NM\_138298)

is another VGAM1671 host target gene. MUC4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MUC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC4 BINDING SITE, designated SEQ ID:28709, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56445] Another function of VGAM1671 is therefore inhibition of Mucin 4, Tracheobronchial (MUC4, Accession NM\_138298), a gene which may act as a ligand for ErbB2 mediated cell signalling. Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC4. The function of MUC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1290.P21/Cdc42/Rac1-activated Kinase 1 (STE20 homolog, yeast) (PAK1, Accession NM\_002576) is another VGAM1671 host target gene. PAK1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PAK1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAK1 BINDING SITE, designated SEQ ID:8434, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56446] Another function of VGAM1671 is therefore inhibition of P21/Cdc42/Rac1-activated Kinase 1 (STE20 homolog, yeast) (PAK1, Accession NM\_002576), a gene which activates the Jun N-terminal kinase MAP kinase pathway. Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK1. The function of PAK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1621. RalA Binding Protein 1 (RALBP1, Accession NM\_006788) is another VGAM1671 host target gene. RALBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RALBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RALBP1 BINDING SITE, des-

ignated SEQ ID:13666, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56447] Another function of VGAM1671 is therefore inhibition of RalA Binding Protein 1 (RALBP1, Accession NM\_006788), a gene which plays a role in signal transduction and catalyzes the transport of glutathione conjugates and xenobiotics. Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RALBP1. The function of RALBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM345. Sex Comb On Midleg-like 2 (Drosophila) (SCML2, Accession NM\_006089) is another VGAM1671 host target gene. SCML2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCML2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCML2 BINDING SITE, designated SEQ ID:12736, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ

ID:4382.

[56448] Another function of VGAM1671 is therefore inhibition of Sex Comb On Midleg-like 2 (*Drosophila*) (SCML2, Accession NM\_006089). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCML2. SH2 Domain Containing Phosphatase Anchor Protein 1 (SPAP1, Accession NM\_030764) is another VGAM1671 host target gene. SPAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPAP1 BINDING SITE, designated SEQ ID:25049, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56449] Another function of VGAM1671 is therefore inhibition of SH2 Domain Containing Phosphatase Anchor Protein 1 (SPAP1, Accession NM\_030764), a gene which regulation of immunologic function. Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPAP1.



The function of SPAP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM672. Chromosome 11 Open Reading Frame 15 (C11orf15, Accession NM\_020644) is another VGAM1671 host target gene. C11orf15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C11orf15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf15 BINDING SITE, designated SEQ ID:21807, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56450] Another function of VGAM1671 is therefore inhibition of Chromosome 11 Open Reading Frame 15 (C11orf15, Accession NM\_020644). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf15. Chromosome 21 Open Reading Frame 42 (C21orf42, Accession NM\_058184) is another VGAM1671 host target gene. C21orf42 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

C21orf42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf42 BINDING SITE, designated SEQ ID:27748, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56451] Another function of VGAM1671 is therefore inhibition of Chromosome 21 Open Reading Frame 42 (C21orf42, Accession NM\_058184). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf42. CGG Triplet Repeat Binding Protein 1 (CGGBP1, Accession NM\_003663) is another VGAM1671 host target gene. CGGBP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CGGBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGGBP1 BINDING SITE, designated SEQ ID:9742, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56452] Another function of VGAM1671 is therefore inhibition of CGG Triplet Repeat Binding Protein 1 (CGGBP1, Accession NM\_003663). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGGBP1. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 12 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX12, Accession XM\_006936) is another VGAM1671 host target gene. DDX12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX12 BINDING SITE, designated SEQ ID:30025, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56453] Another function of VGAM1671 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 12 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX12, Accession XM\_006936). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX12. Deiodi-

nase, Iodothyronine, Type II (DIO2, Accession NM\_000793) is another VGAM1671 host target gene. DIO2 BINDING SITE1 and DIO2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DIO2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIO2 BINDING SITE1 and DIO2 BINDING SITE2, designated SEQ ID:6457 and SEQ ID:15168 respectively, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56454] Another function of VGAM1671 is therefore inhibition of Deiodinase, Iodothyronine, Type II (DIO2, Accession NM\_000793). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIO2. FLJ10761 (Accession NM\_018208) is another VGAM1671 host target gene. FLJ10761 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of FLJ10761 BINDING SITE, designated SEQ ID:20106, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56455] Another function of VGAM1671 is therefore inhibition of FLJ10761 (Accession NM\_018208). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10761. FLJ20509 (Accession NM\_017851) is another VGAM1671 host target gene. FLJ20509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20509 BINDING SITE, designated SEQ ID:19525, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56456] Another function of VGAM1671 is therefore inhibition of FLJ20509 (Accession NM\_017851). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20509. FYVE and Coiled-coil Domain Containing 1

(FYCO1, Accession NM\_024513) is another VGAM1671 host target gene. FYCO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FYCO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FYCO1 BINDING SITE, designated SEQ ID:23710, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56457] Another function of VGAM1671 is therefore inhibition of FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM\_024513). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FYCO1. Glycoprotein A33 (transmembrane) (GPA33, Accession NM\_005814) is another VGAM1671 host target gene. GPA33 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPA33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPA33 BINDING SITE, designated SEQ

ID:12402, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56458] Another function of VGAM1671 is therefore inhibition of Glycoprotein A33 (transmembrane) (GPA33, Accession NM\_005814). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPA33. KIAA0258 (Accession NM\_014785) is another VGAM1671 host target gene. KIAA0258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0258 BINDING SITE, designated SEQ ID:16649, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56459] Another function of VGAM1671 is therefore inhibition of KIAA0258 (Accession NM\_014785). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0258. KIAA0326 (Accession XM\_034819) is another

VGAM1671 host target gene. KIAA0326 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0326, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0326 BINDING SITE, designated SEQ ID:32159, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56460] Another function of VGAM1671 is therefore inhibition of KIAA0326 (Accession XM\_034819). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0326. KIAA0939 (Accession XM\_030524) is another VGAM1671 host target gene. KIAA0939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0939 BINDING SITE, designated SEQ ID:31068, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.



[56461] Another function of VGAM1671 is therefore inhibition of KIAA0939 (Accession XM\_030524). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0939. KIAA1853 (Accession XM\_045184) is another VGAM1671 host target gene. KIAA1853 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1853 BINDING SITE, designated SEQ ID:34389, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56462] Another function of VGAM1671 is therefore inhibition of KIAA1853 (Accession XM\_045184). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1853. MDS028 (Accession NM\_018463) is another VGAM1671 host target gene. MDS028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MDS028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MDS028 BINDING SITE, designated SEQ ID:20536, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56463] Another function of VGAM1671 is therefore inhibition of MDS028 (Accession NM\_018463). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MDS028. Mesoderm Development Candidate 2 (MESDC2, Accession XM\_051854) is another VGAM1671 host target gene. MESDC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MESDC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MESDC2 BINDING SITE, designated SEQ ID:35894, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56464] Another function of VGAM1671 is therefore inhibition of Mesoderm Development Candidate 2 (MESDC2, Accession XM\_051854). Accordingly, utilities of VGAM1671 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with MESDC2. NDRG Family Member 4 (NDRG4, Accession NM\_022910) is another VGAM1671 host target gene. NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NDRG4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2, designated SEQ ID:23216 and SEQ ID:21701 respectively, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56465] Another function of VGAM1671 is therefore inhibition of NDRG Family Member 4 (NDRG4, Accession NM\_022910). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG4. Rho-related BTB Domain Containing 2 (RHOBTB2, Accession XM\_027679) is another VGAM1671 host target gene. RHOBTB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RHOBTB2, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHOBTB2 BINDING SITE, designated SEQ ID:30558, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56466] Another function of VGAM1671 is therefore inhibition of Rho-related BTB Domain Containing 2 (RHOBTB2, Accession XM\_027679). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHOBTB2. Synaptotagmin-like 4 (granuphilin-a) (SYTL4, Accession NM\_080737) is another VGAM1671 host target gene. SYTL4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SYTL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYTL4 BINDING SITE, designated SEQ ID:28024, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56467] Another function of VGAM1671 is therefore inhibition of Synaptotagmin-like 4 (granuphilin-a) (SYTL4, Accession

NM\_080737). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYTL4. Tripartite Motif-containing 38 (TRIM38, Accession NM\_006355) is another VGAM1671 host target gene. TRIM38 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM38, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM38 BINDING SITE, designated SEQ ID:13050, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56468] Another function of VGAM1671 is therefore inhibition of Tripartite Motif-containing 38 (TRIM38, Accession NM\_006355). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM38. LOC122970 (Accession XM\_058672) is another VGAM1671 host target gene. LOC122970 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122970 BINDING SITE, designated SEQ ID:36715, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56469] Another function of VGAM1671 is therefore inhibition of LOC122970 (Accession XM\_058672). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122970. LOC126755 (Accession XM\_059074) is another VGAM1671 host target gene. LOC126755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126755, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126755 BINDING SITE, designated SEQ ID:36857, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56470] Another function of VGAM1671 is therefore inhibition of LOC126755 (Accession XM\_059074). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC126755. LOC126782 (Accession XM\_059080) is another VGAM1671 host target gene. LOC126782 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC126782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126782 BINDING SITE, designated SEQ ID:36860, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56471] Another function of VGAM1671 is therefore inhibition of LOC126782 (Accession XM\_059080). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126782. LOC144742 (Accession XM\_084949) is another VGAM1671 host target gene. LOC144742 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144742, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144742 BINDING SITE, designated SEQ ID:37779, to the nucleotide sequence of VGAM1671 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4382.

[56472] Another function of VGAM1671 is therefore inhibition of LOC144742 (Accession XM\_084949). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144742. LOC145468 (Accession XM\_057874) is another VGAM1671 host target gene. LOC145468 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145468 BINDING SITE, designated SEQ ID:36548, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56473] Another function of VGAM1671 is therefore inhibition of LOC145468 (Accession XM\_057874). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145468. LOC150155 (Accession XM\_047977) is another VGAM1671 host target gene. LOC150155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150155, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150155 BINDING SITE, designated SEQ ID:35089, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56474] Another function of VGAM1671 is therefore inhibition of LOC150155 (Accession XM\_047977). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150155. LOC152503 (Accession XM\_098238) is another VGAM1671 host target gene. LOC152503 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152503, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152503 BINDING SITE, designated SEQ ID:41518, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56475] Another function of VGAM1671 is therefore inhibition of LOC152503 (Accession XM\_098238). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC152503. LOC153577 (Accession XM\_098394) is another VGAM1671 host target gene. LOC153577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153577 BINDING SITE, designated SEQ ID:41647, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56476] Another function of VGAM1671 is therefore inhibition of LOC153577 (Accession XM\_098394). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153577. LOC154428 (Accession XM\_098528) is another VGAM1671 host target gene. LOC154428 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154428, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154428 BINDING SITE, designated SEQ ID:41702, to

the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56477] Another function of VGAM1671 is therefore inhibition of LOC154428 (Accession XM\_098528). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154428. LOC163081 (Accession XM\_091987) is another VGAM1671 host target gene. LOC163081 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163081, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163081 BINDING SITE, designated SEQ ID:40086, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56478] Another function of VGAM1671 is therefore inhibition of LOC163081 (Accession XM\_091987). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163081. LOC196872 (Accession XM\_113760) is another VGAM1671 host target gene. LOC196872 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC196872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196872 BINDING SITE, designated SEQ ID:42418, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56479] Another function of VGAM1671 is therefore inhibition of LOC196872 (Accession XM\_113760). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196872. LOC199232 (Accession XM\_114336) is another VGAM1671 host target gene. LOC199232 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199232 BINDING SITE, designated SEQ ID:42881, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56480] Another function of VGAM1671 is therefore inhibition of LOC199232 (Accession XM\_114336). Accordingly, utilities

of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199232. LOC219401 (Accession XM\_166706) is another VGAM1671 host target gene. LOC219401 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219401 BINDING SITE, designated SEQ ID:44586, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56481] Another function of VGAM1671 is therefore inhibition of LOC219401 (Accession XM\_166706). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219401. LOC221495 (Accession XM\_168136) is another VGAM1671 host target gene. LOC221495 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC221495 BINDING SITE, designated SEQ ID:45058, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56482] Another function of VGAM1671 is therefore inhibition of LOC221495 (Accession XM\_168136). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221495. LOC255565 (Accession XM\_170811) is another VGAM1671 host target gene. LOC255565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255565 BINDING SITE, designated SEQ ID:45588, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56483] Another function of VGAM1671 is therefore inhibition of LOC255565 (Accession XM\_170811). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255565. LOC51580 (Accession NM\_015874) is another VGAM1671 host target gene. LOC51580 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51580 BINDING SITE, designated SEQ ID:18011, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56484] Another function of VGAM1671 is therefore inhibition of LOC51580 (Accession NM\_015874). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51580. LOC90010 (Accession XM\_028150) is another VGAM1671 host target gene. LOC90010 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90010 BINDING SITE, designated SEQ ID:30621, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56485] Another function of VGAM1671 is therefore inhibition of

LOC90010 (Accession XM\_028150). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90010. LOC90249 (Accession XM\_030300) is another VGAM1671 host target gene. LOC90249 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90249 BINDING SITE, designated SEQ ID:31013, to the nucleotide sequence of VGAM1671 RNA, herein designated VGAM RNA, also designated SEQ ID:4382.

[56486] Another function of VGAM1671 is therefore inhibition of LOC90249 (Accession XM\_030300). Accordingly, utilities of VGAM1671 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1672 (VGAM1672) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes



is known in the art.

[56487] VGAM1672 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1672 was detected is described hereinabove with reference to Figs. 1–8.

[56488] VGAM1672 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tick-borne Encephalitis Virus. VGAM1672 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56489] VGAM1672 gene encodes a VGAM1672 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1672 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1672 precursor RNA is designated SEQ ID:1658, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1658 is located at position 9955 relative to the genome of Tick-borne Encephalitis Virus.

[56490] VGAM1672 precursor RNA folds onto itself, forming VGAM1672 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56491] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1672 folded precursor RNA into VGAM1672 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 89%) nucleotide sequence of VGAM1672 RNA is designated SEQ ID:4383, and is provided hereinbelow with reference to the sequence listing part.

[56492] VGAM1672 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1672 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1672 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[56493] VGAM1672 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1672 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1672 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1672 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1672 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[56494] The complementary binding of VGAM1672 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1672 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1672 host target RNA into VGAM1672 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56495] It is appreciated that VGAM1672 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1672 host target genes. The mRNA of each one of this plurality of VGAM1672 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1672 RNA, herein designated VGAM RNA, and which when bound by VGAM1672 RNA causes inhibition of translation of respective one or more VGAM1672 host target proteins.

[56496] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1672 gene, herein designated VGAM GENE, on one

or more VGAM1672 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56497] It is yet further appreciated that a function of VGAM1672 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1672 include diagnosis, prevention and treatment of viral infection by Tick-borne Encephalitis Virus. Specific functions, and accordingly utilities, of VGAM1672 correlate with, and may be deduced from, the identity of the host target genes which VGAM1672 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56498] Nucleotide sequences of the VGAM1672 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1672 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1672 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1672 are further described hereinbelow with reference to Table 1.

[56499] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1672 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1672 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56500] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1672 gene, herein designated VGAM is inhibition of expression of VGAM1672 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1672 correlate with, and may be deduced from, the identity of the target genes which VGAM1672 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56501] KIAA0089 (Accession XM\_046056) is a VGAM1672 host

target gene. KIAA0089 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0089, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0089 BINDING SITE, designated SEQ ID:34668, to the nucleotide sequence of VGAM1672 RNA, herein designated VGAM RNA, also designated SEQ ID:4383.

[56502] A function of VGAM1672 is therefore inhibition of KIAA0089 (Accession XM\_046056). Accordingly, utilities of VGAM1672 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0089. KIAA0227 (Accession XM\_027236) is another VGAM1672 host target gene. KIAA0227 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0227, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0227 BINDING SITE, designated SEQ ID:30455, to the nucleotide sequence of VGAM1672 RNA, herein designated VGAM RNA, also designated SEQ ID:4383.

[56503] Another function of VGAM1672 is therefore inhibition of KIAA0227 (Accession XM\_027236). Accordingly, utilities of VGAM1672 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0227. KIAA1708 (Accession XM\_040211) is another VGAM1672 host target gene. KIAA1708 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1708, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1708 BINDING SITE, designated SEQ ID:33272, to the nucleotide sequence of VGAM1672 RNA, herein designated VGAM RNA, also designated SEQ ID:4383.

[56504] Another function of VGAM1672 is therefore inhibition of KIAA1708 (Accession XM\_040211). Accordingly, utilities of VGAM1672 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1708. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1673 (VGAM1673) viral gene, which modulates expression of respective host target genes



thereof, the function and utility of which host target genes is known in the art.

[56505] VGAM1673 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1673 was detected is described hereinabove with reference to Figs. 1–8.

[56506] VGAM1673 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tick-borne Encephalitis Virus. VGAM1673 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56507] VGAM1673 gene encodes a VGAM1673 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1673 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1673 precursor RNA is designated SEQ ID:1659, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1659 is located at position 6145 relative to the genome of Tick-borne Encephalitis Virus.

[56508] VGAM1673 precursor RNA folds onto itself, forming VGAM1673 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56509] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1673 folded precursor RNA into VGAM1673 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1673 RNA is designated SEQ ID:4384, and is provided hereinbelow with reference to the sequence listing part.

[56510] VGAM1673 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1673 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1673 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56511] VGAM1673 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1673 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1673 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1673 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1673 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56512] The complementary binding of VGAM1673 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1673 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1673 host target RNA into VGAM1673 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56513] It is appreciated that VGAM1673 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1673 host target genes. The mRNA of each one of this plurality of VGAM1673 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1673 RNA, herein designated VGAM RNA, and which when bound by VGAM1673 RNA causes inhibition of translation of respective one or more VGAM1673 host target proteins.

[56514] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1673 gene, herein designated VGAM GENE, on one or more VGAM1673 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56515] It is yet further appreciated that a function of VGAM1673 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of viral infection by Tick-borne Encephalitis Virus. Specific functions, and accordingly utilities, of VGAM1673 correlate with, and may be deduced from, the identity of the host target genes which VGAM1673 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[56516] Nucleotide sequences of the VGAM1673 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1673 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1673 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1673 are further described hereinbelow with reference to Table 1.

[56517] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1673 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1673 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56518] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1673 gene, herein designated VGAM is inhibition of expression of VGAM1673 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1673 correlate with, and may be deduced from, the identity of the target genes which VGAM1673 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56519] Alcohol Dehydrogenase 4 (class II), Pi Polypeptide (ADH4, Accession NM\_000670) is a VGAM1673 host target gene. ADH4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ADH4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADH4 BINDING SITE, designated SEQ ID:6321, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56520] A function of VGAM1673 is therefore inhibition of Alcohol Dehydrogenase 4 (class II), Pi Polypeptide (ADH4, Accession NM\_000670). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADH4. Ankyrin 3, Node of Ranvier (ankyrin G) (ANK3, Accession NM\_020987) is another VGAM1673 host target gene. ANK3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ANK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK3 BINDING SITE, designated SEQ ID:21981, to the nucleotide se-

quence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56521] Another function of VGAM1673 is therefore inhibition of Ankyrin 3, Node of Ranvier (ankyrin G) (ANK3, Accession NM\_020987), a gene which plays key roles in activities such as cell motility, activation, proliferation. Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK3. The function of ANK3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1527. Copine III (CPNE3, Accession NM\_003909) is another VGAM1673 host target gene. CPNE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPNE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPNE3 BINDING SITE, designated SEQ ID:9991, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56522] Another function of VGAM1673 is therefore inhibition of Copine III (CPNE3, Accession NM\_003909), a gene which



may function in membrane trafficking. Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPNE3. The function of CPNE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. V-jun Sarcoma Virus 17 Oncogene Homolog (avian) (JUN, Accession NM\_002228) is another VGAM1673 host target gene. JUN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JUN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JUN BINDING SITE, designated SEQ ID:8009, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56523] Another function of VGAM1673 is therefore inhibition of V-jun Sarcoma Virus 17 Oncogene Homolog (avian) (JUN, Accession NM\_002228), a gene which binds and recognizes the enhancer dna sequencetga(c/g)tca. Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with JUN. The function of JUN has been established by previous studies. The oncogene JUN is the putative transforming gene of avian sarcoma virus 17; it appears to be derived from a gene of the chicken genome and has homologs in several other vertebrate species. (The name JUN comes from the Japanese 'ju-nana,' meaning the number 17.) JUN was originally thought to be identical to the transcription factor AP1. However, it is now known that AP1 is not a single protein, but constitutes a group of related dimeric basic region-leucine zipper proteins that belong to the JUN, FOS (OMIM Ref. No. 164810), MAF (OMIM Ref. No. 177075), and ATF (see OMIM Ref. No. 603148) subfamilies. The various dimers recognize either 12-O-tetradecanoylphorbol-13-acetate (TPA) response elements or cAMP response elements. JUN is the most potent transcriptional activator in its group, and its transcriptional activity is attenuated and sometimes antagonized by JUNB (OMIM Ref. No. 165161). For a review of the structure and function of the AP1 transcription complexes Using a Drosophila model synapse, Sanyal et al. (2002) analyzed cellular functions and regulation of the immediate-early transcription factor AP1, a heterodimer of the basic leucine zipper proteins FOS and JUN. They observed

that AP1 positively regulates synaptic strength and synapse number, thus showing a greater range of influence than CREB (OMIM Ref. No. 123810). Observations from genetic epistasis and RNA quantification experiments indicate that AP1 acts upstream of CREB, regulates levels of CREB mRNA, and functions at the top of the hierarchy of transcription factors known to regulate long-term plasticity. A JUN-kinase signaling module provided a CREB-independent route for neuronal AP1 activation; thus, CREB regulation of AP1 expression may, in some neurons, constitute a positive feedback loop rather than the primary step in AP1 activation. Mathas et al. (2002) found AP1 constitutively activated, with robust JUN and JUNB overexpression, in all cell lines derived from patients with classical Hodgkin lymphoma (OMIM Ref. No. 236000) and anaplastic large cell lymphoma (ALCL), but not in other lymphoma types. AP1 supported proliferation of Hodgkin cells, but suppressed apoptosis of ALCL cells. Mathas et al. (2002) noted that, whereas JUN is upregulated by an autoregulatory process, JUNB is under the control of nuclear factor kappa-B (NFKB; 164011). They found that AP1 and NFKB cooperate and stimulate expression of the cell cycle regulator cyclin D2 (OMIM Ref. No.

123833), the protooncogene MET (OMIM Ref. No. 164860), and the lymphocyte homing receptor CCR7 (OMIM Ref. No. 600242), which are all strongly expressed in primary Hodgkin/Reed–Sternberg (HRS) cells.

[56524] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56525] Sanyal, S.; Sandstrom, D. J.; Hoeffler, C. A.; Ramaswami, M. : AP–1 function upstream of CREB to control synaptic plasticity in *Drosophila*. *Nature* 416: 870–874, 2002. ; and

[56526] Mathas, S.; Hinz, M.; Anagnostopoulos, I.; Krappmann, D.; Lietz, A.; Jundt, F.; Bommert, K.; Mehta–Grigoriou, F.; Stein, H.; Dorken, B.; Scheidereit, C. : Aberrantly expressed c–Jun an.

[56527] Further studies establishing the function and utilities of JUN are found in John Hopkins OMIM database record ID 165160, and in cited publications numbered 4959, 5112–511 and 12745–5121 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Phosphatase 2 (formerly 2A), Regulatory Subunit B (PR 52), Beta Isoform (PPP2R2B, Accession NM\_004576) is another VGAM1673 host target gene. PPP2R2B BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by PPP2R2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R2B BINDING SITE, designated SEQ ID:10921, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56528] Another function of VGAM1673 is therefore inhibition of Protein Phosphatase 2 (formerly 2A), Regulatory Subunit B (PR 52), Beta Isoform (PPP2R2B, Accession NM\_004576). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R2B. Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM\_041375) is another VGAM1673 host target gene. C6orf37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf37 BINDING SITE, designated SEQ ID:33508, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM

RNA, also designated SEQ ID:4384.

[56529] Another function of VGAM1673 is therefore inhibition of Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM\_041375). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf37. Cyclin M1 (CNNM1, Accession NM\_020348) is another VGAM1673 host target gene. CNNM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM1 BINDING SITE, designated SEQ ID:21603, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56530] Another function of VGAM1673 is therefore inhibition of Cyclin M1 (CNNM1, Accession NM\_020348). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM1. Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295) is another VGAM1673 host target gene. EPB41L1 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by EPB41L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L1 BINDING SITE, designated SEQ ID:34935, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56531] Another function of VGAM1673 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L1. FLJ10350 (Accession XM\_170946) is another VGAM1673 host target gene. FLJ10350 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10350 BINDING SITE, designated SEQ ID:45731, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56532] Another function of VGAM1673 is therefore inhibition of FLJ10350 (Accession XM\_170946). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10350. FLJ10420 (Accession NM\_018090) is another VGAM1673 host target gene. FLJ10420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10420 BINDING SITE, designated SEQ ID:19854, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56533] Another function of VGAM1673 is therefore inhibition of FLJ10420 (Accession NM\_018090). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10420. FLJ13213 (Accession NM\_024755) is another VGAM1673 host target gene. FLJ13213 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13213 BINDING SITE, designated SEQ ID:24098, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56534] Another function of VGAM1673 is therefore inhibition of FLJ13213 (Accession NM\_024755). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13213. FLJ13964 (Accession NM\_032186) is another VGAM1673 host target gene. FLJ13964 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13964 BINDING SITE, designated SEQ ID:25900, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56535] Another function of VGAM1673 is therefore inhibition of FLJ13964 (Accession NM\_032186). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ13964. 5'-nucleotidase, Cytosolic IB (NT5C1B, Accession XM\_048837) is another VGAM1673 host target gene. NT5C1B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NT5C1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NT5C1B BINDING SITE, designated SEQ ID:35283, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56536] Another function of VGAM1673 is therefore inhibition of 5'-nucleotidase, Cytosolic IB (NT5C1B, Accession XM\_048837). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NT5C1B. PRO2133 (Accession NM\_018619) is another VGAM1673 host target gene. PRO2133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2133 BINDING SITE, designated

SEQ ID:20689, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56537] Another function of VGAM1673 is therefore inhibition of PRO2133 (Accession NM\_018619). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2133. LOC132332 (Accession XM\_072306) is another VGAM1673 host target gene. LOC132332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC132332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132332 BINDING SITE, designated SEQ ID:37485, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56538] Another function of VGAM1673 is therefore inhibition of LOC132332 (Accession XM\_072306). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132332. LOC146713 (Accession XM\_097071) is another VGAM1673 host target gene. LOC146713 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146713 BINDING SITE, designated SEQ ID:40713, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56539] Another function of VGAM1673 is therefore inhibition of LOC146713 (Accession XM\_097071). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146713. LOC146952 (Accession XM\_097138) is another VGAM1673 host target gene. LOC146952 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146952, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146952 BINDING SITE, designated SEQ ID:40766, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56540] Another function of VGAM1673 is therefore inhibition of

LOC146952 (Accession XM\_097138). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146952. LOC148166 (Accession XM\_086077) is another VGAM1673 host target gene. LOC148166 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148166 BINDING SITE, designated SEQ ID:38479, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56541] Another function of VGAM1673 is therefore inhibition of LOC148166 (Accession XM\_086077). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148166. LOC150174 (Accession XM\_086802) is another VGAM1673 host target gene. LOC150174 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC150174 BINDING SITE, designated SEQ ID:38868, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56542] Another function of VGAM1673 is therefore inhibition of LOC150174 (Accession XM\_086802). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150174. LOC152620 (Accession XM\_011108) is another VGAM1673 host target gene. LOC152620 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152620 BINDING SITE, designated SEQ ID:30172, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56543] Another function of VGAM1673 is therefore inhibition of LOC152620 (Accession XM\_011108). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152620. LOC166042 (Accession XM\_093623) is an-

other VGAM1673 host target gene. LOC166042 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC166042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166042 BINDING SITE, designated SEQ ID:40201, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56544] Another function of VGAM1673 is therefore inhibition of LOC166042 (Accession XM\_093623). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166042. LOC206836 (Accession XM\_116750) is another VGAM1673 host target gene. LOC206836 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC206836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC206836 BINDING SITE, designated SEQ ID:43124, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56545] Another function of VGAM1673 is therefore inhibition of LOC206836 (Accession XM\_116750). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC206836. LOC90520 (Accession XM\_032277) is another VGAM1673 host target gene. LOC90520 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90520 BINDING SITE, designated SEQ ID:31630, to the nucleotide sequence of VGAM1673 RNA, herein designated VGAM RNA, also designated SEQ ID:4384.

[56546] Another function of VGAM1673 is therefore inhibition of LOC90520 (Accession XM\_032277). Accordingly, utilities of VGAM1673 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90520. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1674 (VGAM1674) viral gene, which modulates expression of respective host target genes



thereof, the function and utility of which host target genes is known in the art.

[56547] VGAM1674 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1674 was detected is described hereinabove with reference to Figs. 1–8.

[56548] VGAM1674 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tick-borne Encephalitis Virus. VGAM1674 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56549] VGAM1674 gene encodes a VGAM1674 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1674 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1674 precursor RNA is designated SEQ ID:1660, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1660 is located at position 4389 relative to the genome of Tick-borne Encephalitis Virus.

[56550] VGAM1674 precursor RNA folds onto itself, forming VGAM1674 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56551] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1674 folded precursor RNA into VGAM1674 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1674 RNA is designated SEQ ID:4385, and is provided hereinbelow with reference to the sequence listing part.

[56552] VGAM1674 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1674 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1674 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56553] VGAM1674 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1674 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1674 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1674 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1674 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56554] The complementary binding of VGAM1674 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1674 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1674 host target RNA into VGAM1674 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56555] It is appreciated that VGAM1674 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1674 host target genes. The mRNA of each one of this plurality of VGAM1674 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1674 RNA, herein designated VGAM RNA, and which when bound by VGAM1674 RNA causes inhibition of translation of respective one or more VGAM1674 host target proteins.

[56556] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1674 gene, herein designated VGAM GENE, on one or more VGAM1674 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56557] It is yet further appreciated that a function of VGAM1674 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1674 include diagnosis, prevention and treatment of viral infection by Tick-borne Encephalitis Virus. Specific functions, and accordingly utilities, of VGAM1674 correlate with, and may be deduced from, the identity of the host target genes which VGAM1674 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[56558] Nucleotide sequences of the VGAM1674 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1674 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1674 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1674 are further described hereinbelow with reference to Table 1.

[56559] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1674 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1674 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56560] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1674 gene, herein designated VGAM is inhibition of expression of VGAM1674 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1674 correlate with, and may be deduced from, the identity of the target genes which VGAM1674 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56561] Ephrin-B1 (EFNB1, Accession NM\_004429) is a VGAM1674 host target gene. EFNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNB1 BINDING SITE, designated SEQ ID:10705, to the nucleotide sequence of VGAM1674 RNA, herein designated VGAM RNA, also designated SEQ ID:4385.

[56562] A function of VGAM1674 is therefore inhibition of Ephrin-B1 (EFNB1, Accession NM\_004429), a gene which is a transmembrane ligand of Eph-related receptor tyrosine kinases, has a role in cell adhesion. Accordingly, utilities of VGAM1674 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNB1. The function of EFNB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM390. Peptidylprolyl Isomerase F (cyclophilin F) (PPIF, Accession NM\_005729) is another VGAM1674 host target gene. PPIF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by PPIF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPIF BINDING SITE, designated SEQ ID:12284, to the nucleotide sequence of VGAM1674 RNA, herein designated VGAM RNA, also designated SEQ ID:4385.

[56563] Another function of VGAM1674 is therefore inhibition of Peptidylprolyl Isomerase F (cyclophilin F) (PPIF, Accession NM\_005729), a gene which catalyzes the cis to trans isomerization of certain proline imidic peptide bonds in oligopeptides. Accordingly, utilities of VGAM1674 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPIF. The function of PPIF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM251. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1675 (VGAM1675) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[56564] VGAM1675 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1675 was detected is described hereinabove with reference to Figs. 1–8.

[56565] VGAM1675 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Viral Hemorrhagic Septicemia Virus. VGAM1675 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56566] VGAM1675 gene encodes a VGAM1675 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1675 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1675 precursor RNA is designated SEQ ID:1661, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1661 is located at position 1531 relative to the genome of Viral Hemorrhagic Septicemia Virus.

[56567] VGAM1675 precursor RNA folds onto itself, forming VGAM1675 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56568] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1675 folded precursor RNA into VGAM1675 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1675 RNA is designated SEQ ID:4386, and is provided hereinbelow with reference to the sequence listing part.

[56569] VGAM1675 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1675 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1675 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[56570] VGAM1675 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1675 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1675 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1675 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1675 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56571] The complementary binding of VGAM1675 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1675 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1675 host target RNA into VGAM1675 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56572] It is appreciated that VGAM1675 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1675 host target genes. The mRNA of each one of this plurality of VGAM1675 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1675 RNA, herein designated VGAM RNA, and which when bound by VGAM1675 RNA causes inhibition of translation of respective one or more VGAM1675 host target proteins.

[56573] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1675 gene, herein designated VGAM GENE, on one or more VGAM1675 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56574] It is yet further appreciated that a function of VGAM1675 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1675 include diagnosis, prevention and treatment of viral infection by Viral Hemorrhagic Septicemia Virus. Specific functions, and accordingly utilities, of VGAM1675 correlate with, and may be deduced from, the identity of the host target genes which VGAM1675 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56575] Nucleotide sequences of the VGAM1675 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1675 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1675 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1675 are further  
described hereinbelow with reference to Table 1.

[56576] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1675 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1675 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[56577] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1675 gene, herein designated VGAM is  
inhibition of expression of VGAM1675 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1675 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1675  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[56578] RB1-inducible Coiled-coil 1 (RB1CC1, Accession  
NM\_014781) is a VGAM1675 host target gene. RB1CC1

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RB1CC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RB1CC1 BINDING SITE, designated SEQ ID:16630, to the nucleotide sequence of VGAM1675 RNA, herein designated VGAM RNA, also designated SEQ ID:4386.

[56579] A function of VGAM1675 is therefore inhibition of RB1-inducible Coiled-coil 1 (RB1CC1, Accession NM\_014781), a gene which is likely to participate in nuclear architecture by connecting chromatin with the nuclear matrix or envelope. Accordingly, utilities of VGAM1675 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RB1CC1. The function of RB1CC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18.BCE-1 (Accession NM\_007005) is another VGAM1675 host target gene. BCE-1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BCE-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCE-1 BINDING SITE, designated SEQ ID:13867, to the nucleotide sequence of VGAM1675 RNA, herein designated VGAM RNA, also designated SEQ ID:4386.

[56580] Another function of VGAM1675 is therefore inhibition of BCE-1 (Accession NM\_007005). Accordingly, utilities of VGAM1675 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCE-1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1676 (VGAM1676) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56581] VGAM1676 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1676 was detected is described hereinabove with reference to Figs. 1-8.

[56582] VGAM1676 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Viral Hemorrhagic Septicemia Virus. VGAM1676 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-



tained in the human genome.

[56583] VGAM1676 gene encodes a VGAM1676 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1676 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1676 precursor RNA is designated SEQ ID:1662, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1662 is located at position 7506 relative to the genome of Viral Hemorrhagic Septicemia Virus.

[56584] VGAM1676 precursor RNA folds onto itself, forming VGAM1676 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56585] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1676 folded precursor RNA into VGAM1676 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1676 RNA is designated SEQ ID:4387, and is provided hereinbelow with reference to the sequence listing part.

[56586] VGAM1676 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1676 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1676 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56587] VGAM1676 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1676 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1676 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1676 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1676 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56588] The complementary binding of VGAM1676 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1676 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1676 host target RNA into VGAM1676 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56589] It is appreciated that VGAM1676 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1676 host target genes. The mRNA of each one of this plurality of VGAM1676 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1676 RNA, herein designated VGAM RNA, and which when bound by VGAM1676 RNA causes inhibition of translation of respective one or more VGAM1676 host target proteins.

[56590] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1676 gene, herein designated VGAM GENE, on one or more VGAM1676 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56591] It is yet further appreciated that a function of VGAM1676 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of viral infection by Viral Hemorrhagic Septicemia Virus. Specific functions, and accordingly utilities, of VGAM1676 correlate with, and may be deduced from, the identity of the host target genes which VGAM1676 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56592] Nucleotide sequences of the VGAM1676 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1676 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1676 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1676 are further described hereinbelow with reference to Table 1.

[56593] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1676 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1676 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56594] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1676 gene, herein designated VGAM is inhibition of expression of VGAM1676 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1676 correlate with, and may be deduced from, the identity of the target genes which VGAM1676 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56595] Glycosylphosphatidylinositol Specific Phospholipase D1 (GPLD1, Accession XM\_166347) is a VGAM1676 host target gene. GPLD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPLD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPLD1 BINDING SITE, designated SEQ ID:44181, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ

ID:4387.

[56596] A function of VGAM1676 is therefore inhibition of Glycosylphosphatidylinositol Specific Phospholipase D1 (GPLD1, Accession XM\_166347), a gene which hydrolyses the inositol phosphate linkage in proteins anchored by phosphatidylinositol glycans to release these proteins from the membrane. Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPLD1. The function of GPLD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1575. Polymerase (DNA directed), Theta (POLQ, Accession NM\_006596) is another VGAM1676 host target gene. POLQ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POLQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLQ BINDING SITE, designated SEQ ID:13365, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56597] Another function of VGAM1676 is therefore inhibition of

Polymerase (DNA directed), Theta (POLQ, Accession NM\_006596), a gene which enhances untargeted mutagenesis. Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLQ. The function of POLQ and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM922.SET Translocation (myeloid leukemia-associated) (SET, Accession NM\_003011) is another VGAM1676 host target gene. SET BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SET, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SET BINDING SITE, designated SEQ ID:8920, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56598] Another function of VGAM1676 is therefore inhibition of SET Translocation (myeloid leukemia-associated) (SET, Accession NM\_003011). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SET.



Transforming Growth Factor, Beta 3 (TGFB3, Accession NM\_003239) is another VGAM1676 host target gene. TGFB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB3 BINDING SITE, designated SEQ ID:9234, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56599] Another function of VGAM1676 is therefore inhibition of Transforming Growth Factor, Beta 3 (TGFB3, Accession NM\_003239), a gene which is involved in embryogenesis and cell differentiation. Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB3. The function of TGFB3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1126.caspr5 (Accession NM\_138996) is another VGAM1676 host target gene. caspr5 BINDING SITE1 and caspr5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

caspr5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of caspr5 BINDING SITE1 and caspr5 BINDING SITE2, designated SEQ ID:29095 and SEQ ID:28266 respectively, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56600] Another function of VGAM1676 is therefore inhibition of caspr5 (Accession NM\_138996). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with caspr5. KIAA0937 (Accession XM\_166213) is another VGAM1676 host target gene. KIAA0937 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0937 BINDING SITE, designated SEQ ID:44015, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56601] Another function of VGAM1676 is therefore inhibition of

KIAA0937 (Accession XM\_166213). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0937. Lymphocyte Antigen 75 (LY75, Accession NM\_002349) is another VGAM1676 host target gene. LY75 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LY75, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LY75 BINDING SITE, designated SEQ ID:8150, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56602] Another function of VGAM1676 is therefore inhibition of Lymphocyte Antigen 75 (LY75, Accession NM\_002349). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LY75. Organic Cationic Transporter-like 3 (ORCTL3, Accession NM\_004256) is another VGAM1676 host target gene. ORCTL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ORCTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ORCTL3 BINDING SITE, designated SEQ ID:10444, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56603] Another function of VGAM1676 is therefore inhibition of Organic Cationic Transporter-like 3 (ORCTL3, Accession NM\_004256). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ORCTL3. Tripartite Motif-containing 4 (TRIM4, Accession NM\_033017) is another VGAM1676 host target gene. TRIM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM4 BINDING SITE, designated SEQ ID:26903, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56604] Another function of VGAM1676 is therefore inhibition of Tripartite Motif-containing 4 (TRIM4, Accession NM\_033017). Accordingly, utilities of VGAM1676 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM4. LOC127702 (Accession XM\_060619) is another VGAM1676 host target gene. LOC127702 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127702, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127702 BINDING SITE, designated SEQ ID:37182, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56605] Another function of VGAM1676 is therefore inhibition of LOC127702 (Accession XM\_060619). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127702. LOC143310 (Accession XM\_084485) is another VGAM1676 host target gene. LOC143310 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC143310 BINDING SITE, designated SEQ ID:37603, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56606] Another function of VGAM1676 is therefore inhibition of LOC143310 (Accession XM\_084485). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143310. LOC144262 (Accession XM\_084793) is another VGAM1676 host target gene. LOC144262 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144262, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144262 BINDING SITE, designated SEQ ID:37705, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56607] Another function of VGAM1676 is therefore inhibition of LOC144262 (Accession XM\_084793). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144262. LOC144519 (Accession XM\_084890) is another VGAM1676 host target gene. LOC144519 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144519, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144519 BINDING SITE, designated SEQ ID:37754, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56608] Another function of VGAM1676 is therefore inhibition of LOC144519 (Accession XM\_084890). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144519. LOC145790 (Accession XM\_085234) is another VGAM1676 host target gene. LOC145790 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145790, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145790 BINDING SITE, designated SEQ ID:37978, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56609] Another function of VGAM1676 is therefore inhibition of

LOC145790 (Accession XM\_085234). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145790. LOC164382 (Accession XM\_104390) is another VGAM1676 host target gene. LOC164382 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164382 BINDING SITE, designated SEQ ID:42165, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56610] Another function of VGAM1676 is therefore inhibition of LOC164382 (Accession XM\_104390). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164382. LOC168346 (Accession XM\_095010) is another VGAM1676 host target gene. LOC168346 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC168346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC168346 BINDING SITE, designated SEQ ID:40241, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56611] Another function of VGAM1676 is therefore inhibition of LOC168346 (Accession XM\_095010). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168346. LOC197117 (Accession XM\_116989) is another VGAM1676 host target gene. LOC197117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197117 BINDING SITE, designated SEQ ID:43195, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56612] Another function of VGAM1676 is therefore inhibition of LOC197117 (Accession XM\_116989). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197117. LOC255645 (Accession XM\_172967) is an-

other VGAM1676 host target gene. LOC255645 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255645, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255645 BINDING SITE, designated SEQ ID:46223, to the nucleotide sequence of VGAM1676 RNA, herein designated VGAM RNA, also designated SEQ ID:4387.

[56613] Another function of VGAM1676 is therefore inhibition of LOC255645 (Accession XM\_172967). Accordingly, utilities of VGAM1676 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255645. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1677 (VGAM1677) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56614] VGAM1677 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1677 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[56615] VGAM1677 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Viral Hemorrhagic Septicemia Virus. VGAM1677 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56616] VGAM1677 gene encodes a VGAM1677 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1677 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1677 precursor RNA is designated SEQ ID:1663, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1663 is located at position 5586 relative to the genome of Viral Hemorrhagic Septicemia Virus.

[56617] VGAM1677 precursor RNA folds onto itself, forming VGAM1677 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56618] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1677 folded precursor RNA into VGAM1677 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1677 RNA is designated SEQ ID:4388, and is provided hereinbelow with reference to the sequence listing part.

[56619] VGAM1677 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1677 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1677 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56620] VGAM1677 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1677 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1677 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1677 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1677 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56621] The complementary binding of VGAM1677 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1677 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1677 host target RNA into VGAM1677 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56622] It is appreciated that VGAM1677 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1677 host target genes. The mRNA of each one of this plurality of VGAM1677 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1677 RNA, herein designated VGAM RNA, and which when bound by VGAM1677 RNA causes inhibition of translation of respective one or more VGAM1677 host target proteins.

[56623] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1677 gene, herein designated VGAM GENE, on one or more VGAM1677 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56624] It is yet further appreciated that a function of VGAM1677 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of viral infection by Viral Hemorrhagic Septicemia Virus. Specific functions, and accordingly utilities, of VGAM1677 correlate with, and may be deduced from, the identity of the host target genes which VGAM1677 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56625] Nucleotide sequences of the VGAM1677 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1677 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1677 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1677 are further described hereinbelow with reference to Table 1.

[56626] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1677 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1677 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56627] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1677 gene, herein designated VGAM is inhibition of expression of VGAM1677 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1677 correlate with, and may be deduced from, the identity of the target genes which VGAM1677 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56628] Cytochrome P450, 51 (lanosterol 14- $\alpha$ -demethylase) (CYP51, Accession NM\_000786) is a VGAM1677 host target gene. CYP51 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CYP51, corresponding to a HOST TARGET binding site



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP51 BINDING SITE, designated SEQ ID:6436, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56629] A function of VGAM1677 is therefore inhibition of Cytochrome P450, 51 (lanosterol 14- $\alpha$ -demethylase) (CYP51, Accession NM\_000786). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP51. Deoxyribonuclease I-like 1 (DNASE1L1, Accession NM\_006730) is another VGAM1677 host target gene. DNASE1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNASE1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNASE1L1 BINDING SITE, designated SEQ ID:13566, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56630] Another function of VGAM1677 is therefore inhibition of

Deoxyribonuclease I-like 1 (DNASE1L1, Accession NM\_006730), a gene which seems to be involved in cell death. Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNASE1L1. The function of DNASE1L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM885. ELK3, ETS-domain Protein (SRF accessory protein 2) (ELK3, Accession NM\_005230) is another VGAM1677 host target gene. ELK3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ELK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELK3 BINDING SITE, designated SEQ ID:11733, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56631] Another function of VGAM1677 is therefore inhibition of ELK3, ETS-domain Protein (SRF accessory protein 2) (ELK3, Accession NM\_005230), a gene which may be a negative regulator of transcription but can activate transcription

when coexpressed with ras, src or mos. Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELK3. The function of ELK3 has been established by previous studies. The ETS gene family encodes a group of proteins that function as transcription factors under physiologic conditions and, if aberrantly expressed, can cause cellular transformation. Lopez et al. (1994) cloned the gene for a new ETS-related transcription factor, which they called ERP for 'ETS-related protein,' from a murine pre-B cell line and from lung tissue. The ERP protein contained a region of high homology with the ETS DNA-binding domain common to all members of the ETS transcription factor/oncoprotein family. Within the B-cell lineage, ERP is highly expressed primarily at early stages of B-lymphocyte development, and expression declines drastically upon B-cell maturation, correlating with the activity of the enhancer of immunoglobulin heavy chain. The data suggested that ERP plays a role in both B-cell development and IgH gene regulation. Giovane et al. (1994) identified the same ETS family member, which they designated Net, from Ras-transformed mouse fibroblasts using PCR primers based on the nucleotide sequence cor-

responding to the most conserved amino acids of the ETS domain. They subsequently obtained a complete cDNA sequence. The predicted Net protein contains an ETS domain at the amino terminus that is about 80% similar to the human ELK1 (OMIM Ref. No. 311040) and ELK4 (OMIM Ref. No. 600246) sequences. The authors noted that 2 other domains also show significant similarity to regions of these proteins, and that the 3 genes clearly belong to the ELK family. Two mRNAs of 2.5 and 4.5 kb were detected by Northern blotting. Transcripts were found, at varying levels, in a large number of transformed cell lines and tissues. The authors showed that Net protein bound to ETS DNA motifs and could form complexes with SRF (OMIM Ref. No. 600589) on the fos serum response element. Using fluorescence in situ hybridization, Shipley et al. (1994) mapped ELK4 and ELK3 to 1q32 and 12q23, respectively. (The authors referred to ELK4 as SAP1 and to ELK3 as SAP2.) Tamai et al. (1995) mapped the Elk3 gene to mouse chromosome 10 and suggested that the human homolog (ELK3) may be located on 12q in the interval between bands q21 and q24 because of established homology of synteny with the mid-distal region of mouse chromosome 10. Giovane et al. (1995) mapped ELK3 to human

12q22–q23 and to mouse 10C–D1 by in situ hybridization.

[56632] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56633] Giovane, A.; Pintzas, A.; Maira, S.–M.; Sobieszczuk, P.; Wasylyk, B. : Net, a new ets transcription factor that is activated by Ras. *Genes Dev.* 8: 1502–1513, 1994. ; and

[56634] Giovane, A.; Sobieszczuk, P.; Mignon, C.; Mattei, M.–G.; Wasylyk, B. : Locations of the ets subfamily members net, elk1, and sap1 (ELK3, ELK1, and ELK4) on three homologous regions of t.

[56635] Further studies establishing the function and utilities of ELK3 are found in John Hopkins OMIM database record ID 600247, and in cited publications numbered 7921, 862 and 8630 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ectonucleotide Pyrophosphatase/phosphodiesterase 3 (ENPP3, Accession NM\_005021) is another VGAM1677 host target gene. ENPP3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ENPP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENPP3 BINDING SITE, designated SEQ ID:11462, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56636] Another function of VGAM1677 is therefore inhibition of Ectonucleotide Pyrophosphatase/phosphodiesterase 3 (ENPP3, Accession NM\_005021). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENPP3. Glucagon Receptor (GCGR, Accession NM\_000160) is another VGAM1677 host target gene. GCGR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GCGR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCGR BINDING SITE, designated SEQ ID:5664, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56637] Another function of VGAM1677 is therefore inhibition of Glucagon Receptor (GCGR, Accession NM\_000160), a gene which controls the rate of hepatic glucose production and

insulin secretion. Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCGR. The function of GCGR has been established by previous studies. Hager et al. (1995) reported the association of a single heterozygous gly-to-ser missense mutation in the glucagon receptor gene with late-onset noninsulin-dependent diabetes mellitus (OMIM Ref. No. 125853). In a pooled set of French and Sardinian patients, the gly40-to-ser mutation showed association with NIDDM (chi square = 14.4,  $P = 0.0001$ ). In 18 sibships from 9 French pedigrees, some evidence for linkage to diabetes was found. Receptor binding studies using cultured cells expressing the gly40-to-ser mutation demonstrated that this mutation results in a receptor that binds glucagon with a 3-fold lower affinity compared to the wildtype receptor. The physiologic effects of glucagon (GCG; 138030) are mediated through the glucagon receptor, a 480-amino acid protein that is a member of the superfamily of receptors characterized by a 7 transmembrane domain structure and by their coupling via GTP-binding proteins (G-proteins) to adenyl cyclase. Menzel et al. (1994) cloned human glucagon receptor cDNA and demonstrated 85%

nucleotide and 91% amino acid identity with the rat sequence. By fluorescence in situ hybridization, they localized the GCGR gene to 17q25. An Alu variable poly(A) DNA polymorphism was identified in the gene. Use of the polymorphism in a study of CEPH families showed linkage between the polymorphism and markers localized to distal 17q. The receptor for glucagon-like peptide-1 (GLP1R; 138032), which is derived from the same preproglucagon molecule, has structural similarities but does not bind peptides of related structure and similar function, such as glucagon. Lok et al. (1994) isolated a cDNA encoding a complete functional human glucagon receptor from a liver cDNA library by a combination of polymerase chain reaction and colony hybridization. The cDNA encoded a protein that had 80% identity to rat glucagon receptor, bound (125-I)-labeled glucagon, and transduced a signal leading to increases in the concentration of intracellular cyclic AMP. Southern blot analysis of human DNA suggested the presence of a single GCGR locus. By in situ hybridization, Lok et al. (1994) mapped the GCGR locus to 17q25. Analysis of the genomic sequence showed that the coding region spans over 5.5 kb and is interrupted by 12 introns.

[56638] Full details of the abovementioned studies are described



in the following publications, the disclosure of which are hereby incorporated by reference:

[56639] Hager, J.; Hansen, L.; Vaisse, C.; Vionnet, N.; Philippi, A.; Poller, W.; Velho, G.; Carcassi, C.; Contu, L.; Julier, C.; Cambien, F.; Passa, P.; Lathrop, M.; Kindsvogel, W.; Deme-nais, F.; Nishimura, E.; Froguel, P. : A missense mutation in the glucagon receptor gene is associated with non-insulin-dependent diabetes mellitus. *Nature Genet.* 9: 299-304, 1995. ; and

[56640] Lok, S.; Kuijper, J. L.; Jelinek, L. J.; Kramer, J. M.; Whitmore, T. E.; Sprecher, C. A.; Mathewes, S.; Grant, F. J.; Biggs, S. H.; Rosenberg, G. B.; Sheppard, P. O.; O'Hara, P. J.; Fos.

[56641] Further studies establishing the function and utilities of GCGR are found in John Hopkins OMIM database record ID 138033, and in cited publications numbered 335 and 3359-3361 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate Receptor, Ionotropic, Kainate 3 (GRIK3, Accession NM\_000831) is another VGAM1677 host target gene. GRIK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRIK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of GRIK3 BINDING SITE, designated SEQ ID:6485, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56642] Another function of VGAM1677 is therefore inhibition of Glutamate Receptor, Ionotropic, Kainate 3 (GRIK3, Accession NM\_000831). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIK3. Intercellular Adhesion Molecule 1 (CD54), Human Rhinovirus Receptor (ICAM1, Accession XM\_049518) is another VGAM1677 host target gene. ICAM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICAM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICAM1 BINDING SITE, designated SEQ ID:35442, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56643] Another function of VGAM1677 is therefore inhibition of Intercellular Adhesion Molecule 1 (CD54), Human Rhi-

novirus Receptor (ICAM1, Accession XM\_049518), a gene which binds the integrin LFA-1 (ITGB2) and promotes adhesion; member of the immunoglobulin superfamily. Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICAM1. The function of ICAM1 has been established by previous studies. Intercellular adhesion molecule-1 (ICAM1) is a ligand for lymphocyte-function associated (LFA) antigens (see OMIM Ref. No. 116920). Simmons et al. (1988) analyzed a cDNA clone of the ICAM1 gene and found that it showed homology to the neural cell adhesion molecule NCAM (OMIM Ref. No. 116930). Greve et al. (1989) demonstrated that the ICAM1 protein is the major human rhinovirus receptor. Bella et al. (1998) analyzed the structural features of the ICAM1 molecule that underlie its function as a receptor for the major group of human rhinoviruses and as a ligand for LFA-1. Expression of HLA-DR antigen (see OMIM Ref. No. 142860) and ICAM1 in human conjunctival epithelium is upregulated in patients with dry eyes associated with Sjogren syndrome (OMIM Ref. No. 270150). Tsubota et al. (1999) reported that this upregulation in Sjogren syndrome patients may be controlled by interferon-gamma

(OMIM Ref. No. 147570) through the activation of transcription factor NF $\kappa$ B (nuclear OMIM Ref. No. 164011). Pisella et al. (2000) reported that a significant increase of HLA-DR and ICAM1 expression by epithelial cells was consistently found in patients with keratoconjunctivitis sicca (Sjogren syndrome) compared with expression in normal eyes. These 2 markers were well correlated with each other and correlated inversely with tear break-up time and tear production as measured by the Schirmer test. The percentage of conjunctival goblet cells was significantly decreased in dry eye patients with a significant negative correlation with both HLA-DR and ICAM1 markers. Lu and Cyster (2002) studied the mechanisms that control localization of marginal zone B cells. They demonstrated that marginal zone B cells express elevated levels of the integrins LFA-1 (see OMIM Ref. No. 153370) and alpha-4-beta-1 (see OMIM Ref. No. 192975 and 135630), and that the marginal zone B cells bind to the ligands ICAM1 and VCAM1 (OMIM Ref. No. 192225). These ligands are expressed within the marginal zone in a lymphotoxin-dependent manner. Combined inhibition of LFA-1 and alpha-4-beta-1 causes a rapid and selective release of B cells from the marginal zone. Furthermore, lipopolysac-

charide-triggered marginal zone B cell relocation involves downregulation of integrin-mediated adhesion. Lu and Cyster (2002) concluded that their studies identified key requirements for marginal zone B cell localization and established a role for integrins in peripheral lymphoid tissue compartmentalization. Animal model experiments lend further support to the function of ICAM1. To test the role of Icam1 in intact animals, Sligh et al. (1993) disrupted the gene in murine embryonic stem cells by gene targeting. Homozygous deficient animals developed normally, were fertile, and had a moderate granulocytosis. Studies were consistent with complete loss of surface expression of the protein. Deficient mice exhibited prominent abnormalities of inflammatory responses including impaired neutrophil emigration in response to chemical peritonitis and decreased contact hypersensitivity to 2,4-dinitrofluorobenzene. Mutant cells provided negligible stimulation in the mixed lymphocyte reaction, although they proliferated normally as responder cells

[56644] It is appreciated that the abovementioned animal model for ICAM1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

- [56645] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [56646] Sligh, J. E., Jr.; Ballantyne, C. M.; Rich, S. S.; Hawkins, H. K.; Smith, C. W.; Bradley, A.; Beaudet, A. L. : Inflammatory and immune responses are impaired in mice deficient in inter-cellular adhesion molecule 1. Proc. Nat. Acad. Sci. 90: 8529–8533, 1993. ; and
- [56647] Lu, T. T.; Cyster, J. G. : Integrin-mediated long-term B cell retention in the splenic marginal zone. Science 297: 409–412, 2002.
- [56648] Further studies establishing the function and utilities of ICAM1 are found in John Hopkins OMIM database record ID 147840, and in cited publications numbered 3045–3054, 11448, 4813, 3912, 471 and 11450 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. MAX Binding Protein (MNT, Accession NM\_020310) is another VGAM1677 host target gene. MNT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MNT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of MNT BINDING SITE, designated SEQ ID:21559, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56649] Another function of VGAM1677 is therefore inhibition of MAX Binding Protein (MNT, Accession NM\_020310). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MNT. Nitric Oxide Synthase 1 (neuronal) (NOS1, Accession NM\_000620) is another VGAM1677 host target gene. NOS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NOS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NOS1 BINDING SITE, designated SEQ ID:6230, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56650] Another function of VGAM1677 is therefore inhibition of Nitric Oxide Synthase 1 (neuronal) (NOS1, Accession NM\_000620), a gene which produces nitric oxide (no) which is a messenger molecule with diverse functions

throughout the body. Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NOS1. The function of NOS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM323. Amino peptidase Puromycin Sensitive (NPEPPS, Accession NM\_006310) is another VGAM1677 host target gene. NPEPPS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPEPPS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPEPPS BINDING SITE, designated SEQ ID:12997, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56651] Another function of VGAM1677 is therefore inhibition of Amino peptidase Puromycin Sensitive (NPEPPS, Accession NM\_006310), a gene which is puromycin-sensitive aminopeptidase and has metallopeptidase activity. Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions



associated with NPEPPS. The function of NPEPPS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM83. Neurogranin (protein kinase C substrate, RC3) (NRGN, Accession NM\_006176) is another VGAM1677 host target gene. NRGN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NRGN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRGN BINDING SITE, designated SEQ ID:12835, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56652] Another function of VGAM1677 is therefore inhibition of Neurogranin (protein kinase C substrate, RC3) (NRGN, Accession NM\_006176), a gene which acts as a "third messenger" substrate of protein kinase c-mediated molecular cascades during synaptic development and remodeling. Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRGN. The function of NRGN has been established by previous studies. Neurogranin is a

brain-specific protein expressed in telencephalic neurons. Neurogranin was first identified by Baudier et al. (1991) from bovine forebrain. Baudier et al. (1991) showed that, like GAP43 (OMIM Ref. No. 162060), rat neurogranin, also called p17 or RC3, is phosphorylated by protein kinase C (see OMIM Ref. No. 176960) and binds calmodulin in the absence of calcium. Martinez de Arrieta et al. (1997) cloned human neurogranin by screening a placental genomic library with the homologous rat cDNA. The 78-amino acid human protein is 96% identical to rat neurogranin. On Northern blots of human tissues, Martinez de Arrieta et al. (1997) detected neurogranin expression only in brain. Martinez de Arrieta et al. (1997) localized the neurogranin gene to 11q24 based on its inclusion within a YAC from that region. In the rat brain, neurogranin is under thyroid hormone control in specific neuronal subsets in both developing and adult animals. To evaluate whether the human gene is also a target of thyroid hormone, Martinez de Arrieta et al. (1999) searched for T3-responsive elements in NRGN cloned genomic fragments spanning the whole gene. A T3 receptor-binding site was found in the first intron, 3,000 bp downstream from the origin of transcription. Further data re-

ported by Martinez de Arrieta et al. (1999) suggested that NRGN is a direct target for thyroid hormone in human brain, and that control of expression of this gene could underlay many of the consequences of hypothyroidism on mental states during development as well as in adult subjects.

[56653] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56654] Baudier, J.; Deloulme, J. C.; Van Dorsselaer, A.; Black, D.; Matthes, H. W. D. : Purification and characterization of a brain-specific protein kinase C substrate, neurogranin (p17): identification of a consensus amino acid sequence between neurogranin and neuromodulin (GAP43) that corresponds to the protein kinase C phosphorylation site and the calmodulin-binding domain. J. Biol. Chem. 266: 229-237, 1991. ; and

[56655] Martinez de Arrieta, C.; Morte, B.; Coloma, A.; Bernal, J. : The human RC3 gene homolog, NRGN contains a thyroid hormone-responsive element located in the first intron. Endocrinology 14.

[56656] Further studies establishing the function and utilities of NRGN are found in John Hopkins OMIM database record ID

602350, and in cited publications numbered 1017–1014 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. P53AIP1 (Accession NM\_022112) is another VGAM1677 host target gene.

P53AIP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by P53AIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P53AIP1 BINDING SITE, designated SEQ ID:22659, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56657] Another function of VGAM1677 is therefore inhibition of P53AIP1 (Accession NM\_022112). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P53AIP1. Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM\_138694) is another VGAM1677 host target gene. PKHD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PKHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND–

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKHD1 BINDING SITE, designated SEQ ID:28940, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56658] Another function of VGAM1677 is therefore inhibition of Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM\_138694). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKHD1. Vasoactive Intestinal Peptide Receptor 1 (VIPR1, Accession NM\_004624) is another VGAM1677 host target gene. VIPR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VIPR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VIPR1 BINDING SITE, designated SEQ ID:10995, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56659] Another function of VGAM1677 is therefore inhibition of Vasoactive Intestinal Peptide Receptor 1 (VIPR1, Accession

NM\_004624), a gene which binds vip and is mediated by g proteins which activate adenylyl cyclase. Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIPR1. The function of VIPR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM548. Apolipoprotein L, 6 (APOL6, Accession NM\_030641) is another VGAM1677 host target gene. APOL6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by APOL6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL6 BINDING SITE, designated SEQ ID:24970, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56660] Another function of VGAM1677 is therefore inhibition of Apolipoprotein L, 6 (APOL6, Accession NM\_030641). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL6. FLJ20435 (Accession NM\_017821)

is another VGAM1677 host target gene. FLJ20435 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20435 BINDING SITE, designated SEQ ID:19468, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56661] Another function of VGAM1677 is therefore inhibition of FLJ20435 (Accession NM\_017821). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20435. KIAA0247 (Accession NM\_014734) is another VGAM1677 host target gene. KIAA0247 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0247 BINDING SITE, designated SEQ ID:16373, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56662] Another function of VGAM1677 is therefore inhibition of KIAA0247 (Accession NM\_014734). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0247. KIAA0368 (Accession XM\_036708) is another VGAM1677 host target gene. KIAA0368 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0368, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0368 BINDING SITE, designated SEQ ID:32490, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56663] Another function of VGAM1677 is therefore inhibition of KIAA0368 (Accession XM\_036708). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0368. MGC11115 (Accession NM\_032310) is another VGAM1677 host target gene. MGC11115 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11115, corresponding to a HOST TARGET binding site such as BINDING SITE I,



BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11115 BINDING SITE, designated SEQ ID:26099, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56664] Another function of VGAM1677 is therefore inhibition of MGC11115 (Accession NM\_032310). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11115. Nucleoredoxin (NXN, Accession NM\_022463) is another VGAM1677 host target gene. NXN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXN BINDING SITE, designated SEQ ID:22807, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56665] Another function of VGAM1677 is therefore inhibition of Nucleoredoxin (NXN, Accession NM\_022463). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with NXN. Neurexophilin 3 (NXPH3, Accession XM\_037847) is another VGAM1677 host target gene. NXPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXPH3 BINDING SITE, designated SEQ ID:32717, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56666] Another function of VGAM1677 is therefore inhibition of Neurexophilin 3 (NXPH3, Accession XM\_037847). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXPH3. poly(rC) Binding Protein 3 (PCBP3, Accession NM\_020528) is another VGAM1677 host target gene. PCBP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCBP3 BINDING SITE, designated SEQ

ID:21751, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56667] Another function of VGAM1677 is therefore inhibition of poly(rC) Binding Protein 3 (PCBP3, Accession NM\_020528). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCBP3. Retinoic Acid Induced 15 (RAI15, Accession XM\_039548) is another VGAM1677 host target gene. RAI15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI15 BINDING SITE, designated SEQ ID:33119, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56668] Another function of VGAM1677 is therefore inhibition of Retinoic Acid Induced 15 (RAI15, Accession XM\_039548). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI15. Sideroflexin 5 (SFXN5, Acces-

sion NM\_144579) is another VGAM1677 host target gene. SFXN5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SFXN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFXN5 BINDING SITE, designated SEQ ID:29388, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56669] Another function of VGAM1677 is therefore inhibition of Sideroflexin 5 (SFXN5, Accession NM\_144579). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFXN5. SMOC1 (Accession NM\_022137) is another VGAM1677 host target gene. SMOC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SMOC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMOC1 BINDING SITE, designated SEQ ID:22700, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA,

also designated SEQ ID:4388.

[56670] Another function of VGAM1677 is therefore inhibition of SMOC1 (Accession NM\_022137). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMOC1. LOC144519 (Accession XM\_084890) is another VGAM1677 host target gene. LOC144519 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144519, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144519 BINDING SITE, designated SEQ ID:37759, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56671] Another function of VGAM1677 is therefore inhibition of LOC144519 (Accession XM\_084890). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144519. LOC144866 (Accession XM\_096699) is another VGAM1677 host target gene. LOC144866 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144866, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144866 BINDING SITE, designated SEQ ID:40477, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56672] Another function of VGAM1677 is therefore inhibition of LOC144866 (Accession XM\_096699). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144866. LOC149302 (Accession XM\_086489) is another VGAM1677 host target gene. LOC149302 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149302 BINDING SITE, designated SEQ ID:38706, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56673] Another function of VGAM1677 is therefore inhibition of LOC149302 (Accession XM\_086489). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC149302. LOC149373 (Accession XM\_086507) is another VGAM1677 host target gene. LOC149373 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149373 BINDING SITE, designated SEQ ID:38719, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56674] Another function of VGAM1677 is therefore inhibition of LOC149373 (Accession XM\_086507). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149373. LOC150685 (Accession XM\_103563) is another VGAM1677 host target gene. LOC150685 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150685, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150685 BINDING SITE, designated SEQ ID:42155, to

the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56675] Another function of VGAM1677 is therefore inhibition of LOC150685 (Accession XM\_103563). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150685. LOC152274 (Accession XM\_087418) is another VGAM1677 host target gene. LOC152274 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152274 BINDING SITE, designated SEQ ID:39235, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56676] Another function of VGAM1677 is therefore inhibition of LOC152274 (Accession XM\_087418). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152274. LOC163682 (Accession XM\_099402) is another VGAM1677 host target gene. LOC163682 BINDING SITE is HOST TARGET binding site found in the 5' un-



translated region of mRNA encoded by LOC163682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163682 BINDING SITE, designated SEQ ID:42089, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56677] Another function of VGAM1677 is therefore inhibition of LOC163682 (Accession XM\_099402). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163682. LOC90906 (Accession XM\_034809) is another VGAM1677 host target gene. LOC90906 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90906 BINDING SITE, designated SEQ ID:32148, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56678] Another function of VGAM1677 is therefore inhibition of LOC90906 (Accession XM\_034809). Accordingly, utilities

of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90906. LOC91445 (Accession XM\_018516) is another VGAM1677 host target gene. LOC91445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91445 BINDING SITE, designated SEQ ID:30367, to the nucleotide sequence of VGAM1677 RNA, herein designated VGAM RNA, also designated SEQ ID:4388.

[56679] Another function of VGAM1677 is therefore inhibition of LOC91445 (Accession XM\_018516). Accordingly, utilities of VGAM1677 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91445. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1678 (VGAM1678) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56680] VGAM1678 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1678 was detected is described hereinabove with reference to Figs. 1-8.

[56681] VGAM1678 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Viral Hemorrhagic Septicemia Virus. VGAM1678 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56682] VGAM1678 gene encodes a VGAM1678 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1678 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1678 precursor RNA is designated SEQ ID:1664, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1664 is located at position 10783 relative to the genome of Viral Hemorrhagic Septicemia Virus.

[56683] VGAM1678 precursor RNA folds onto itself, forming VGAM1678 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56684] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1678 folded precursor RNA into VGAM1678 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 87%) nucleotide sequence of VGAM1678 RNA is designated SEQ ID:4389, and is provided hereinbelow with reference to the sequence listing part.

[56685] VGAM1678 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1678 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1678 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[56686] VGAM1678 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1678 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1678 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1678 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1678 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56687] The complementary binding of VGAM1678 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1678 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1678 host target RNA into VGAM1678 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56688] It is appreciated that VGAM1678 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1678 host target genes. The mRNA of each one of this plurality of VGAM1678 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1678 RNA, herein designated VGAM RNA, and which when bound by VGAM1678 RNA causes inhibition of translation of respective one or more VGAM1678 host target proteins.

[56689] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1678 gene, herein designated VGAM GENE, on one or more VGAM1678 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56690] It is yet further appreciated that a function of VGAM1678 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of viral infection by Viral Hemorrhagic Septicemia Virus. Specific functions, and accordingly utilities, of VGAM1678 correlate with, and may be deduced from, the identity of the host target genes which VGAM1678 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56691] Nucleotide sequences of the VGAM1678 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1678 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1678 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1678 are further  
described hereinbelow with reference to Table 1.

[56692] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1678 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1678 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[56693] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1678 gene, herein designated VGAM is  
inhibition of expression of VGAM1678 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1678 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1678  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[56694] Phospholipase A2, Group IVC (cytosolic, calcium-in-  
dependent) (PLA2G4C, Accession XM\_055864) is a



VGAM1678 host target gene. PLA2G4C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLA2G4C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2G4C BINDING SITE, designated SEQ ID:36342, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56695] A function of VGAM1678 is therefore inhibition of Phospholipase A2, Group IVC (cytosolic, calcium-independent) (PLA2G4C, Accession XM\_055864), a gene which hydrolyzes the phospholipid sn-2 ester bond. Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLA2G4C. The function of PLA2G4C has been established by previous studies. The cytosolic phospholipases A2 (OMIM Ref. No. cPLA2s) catalyze the release of certain fatty acids from phospholipids and play a role in a wide range of physiologic functions. By searching an EST database to identify sequences similar to cPLA2-alpha (OMIM Ref. No. 600522), Underwood et al. (1998) identified a novel PLA2 homolog, which they named

cPLA2-gamma. They cloned the corresponding cDNA from a human skeletal muscle library. The cPLA2-gamma sequence predicts a 541-amino acid polypeptide with 28% identity to cPLA2-alpha. Expression studies showed that cPLA2-gamma liberates arachidonate from phospholipid, cleaving at either sn-1 or sn-2 sites. cPLA2-gamma is prenylated, membrane-associated, and calcium-independent. Northern blot analysis revealed that cPLA2-gamma is expressed as a 3-kb mRNA most abundantly in skeletal muscle and heart, with lower levels in several other tissues. Using STS analysis, Pickard et al. (1999) mapped the PLA2G4C gene to chromosome 19.

[56696] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56697] Pickard, R. T.; Strifler, B. A.; Kramer, R. M.; Sharp, J. D. : Molecular cloning of two new human paralogs of 85-kDa cytosolic phospholipase A2. J. Biol. Chem. 274: 8823-8831, 1999. ; and

[56698] Underwood, K. W.; Song, C.; Kriz, R. W.; Chang, X. J.; Knopf, J. L.; Lin, L.-L. : A novel calcium-independent phospholipase A(2), cPLA(2)-gamma, that is prenylated and contains homolog.

[56699] Further studies establishing the function and utilities of PLA2G4C are found in John Hopkins OMIM database record ID 603602, and in cited publications numbered 4893 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sel-1 Suppressor of Lin-12-like (C. elegans) (SEL1L, Accession NM\_005065) is another VGAM1678 host target gene. SEL1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEL1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEL1L BINDING SITE, designated SEQ ID:11503, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56700] Another function of VGAM1678 is therefore inhibition of Sel-1 Suppressor of Lin-12-like (C. elegans) (SEL1L, Accession NM\_005065), a gene which may play a role in notch signaling (by similarity). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEL1L. The function of SEL1L and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM245. Baculoviral IAP Repeat-containing 8 (BIRC8, Accession NM\_033341) is another VGAM1678 host target gene. BIRC8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BIRC8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIRC8 BINDING SITE, designated SEQ ID:27194, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56701] Another function of VGAM1678 is therefore inhibition of Baculoviral IAP Repeat-containing 8 (BIRC8, Accession NM\_033341). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC8. C1q and Tumor Necrosis Factor Related Protein 7 (C1QTNF7, Accession NM\_031911) is another VGAM1678 host target gene. C1QTNF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1QTNF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of C1QTNF7 BINDING SITE, designated SEQ ID:25666, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56702] Another function of VGAM1678 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 7 (C1QTNF7, Accession NM\_031911). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF7. DKFZp547I224 (Accession NM\_020221) is another VGAM1678 host target gene. DKFZp547I224 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547I224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I224 BINDING SITE, designated SEQ ID:21478, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56703] Another function of VGAM1678 is therefore inhibition of DKFZp547I224 (Accession NM\_020221). Accordingly, utilities of VGAM1678 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZp547I224. FLJ10120 (Accession NM\_018001) is another VGAM1678 host target gene. FLJ10120 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10120 BINDING SITE, designated SEQ ID:19729, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56704] Another function of VGAM1678 is therefore inhibition of FLJ10120 (Accession NM\_018001). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10120. FLJ11783 (Accession NM\_024891) is another VGAM1678 host target gene. FLJ11783 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11783, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11783 BINDING SITE, designated SEQ ID:24365, to the nucleotide

sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56705] Another function of VGAM1678 is therefore inhibition of FLJ11783 (Accession NM\_024891). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11783. FLJ22174 (Accession NM\_021945) is another VGAM1678 host target gene. FLJ22174 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22174 BINDING SITE, designated SEQ ID:22467, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56706] Another function of VGAM1678 is therefore inhibition of FLJ22174 (Accession NM\_021945). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22174. FLJ23499 (Accession NM\_022761) is another VGAM1678 host target gene. FLJ23499 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by FLJ23499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23499 BINDING SITE, designated SEQ ID:23005, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56707] Another function of VGAM1678 is therefore inhibition of FLJ23499 (Accession NM\_022761). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23499. IKKE (Accession NM\_014002) is another VGAM1678 host target gene. IKKE BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IKKE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IKKE BINDING SITE, designated SEQ ID:15203, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56708] Another function of VGAM1678 is therefore inhibition of IKKE (Accession NM\_014002). Accordingly, utilities of



VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IKKE. KIAA0323 (Accession XM\_032634) is another VGAM1678 host target gene. KIAA0323 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0323 BINDING SITE, designated SEQ ID:31695, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56709] Another function of VGAM1678 is therefore inhibition of KIAA0323 (Accession XM\_032634). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0323. KIAA1161 (Accession XM\_088501) is another VGAM1678 host target gene. KIAA1161 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1161 BINDING SITE, designated SEQ ID:39754, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56710] Another function of VGAM1678 is therefore inhibition of KIAA1161 (Accession XM\_088501). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1161. KIAA1727 (Accession XM\_034262) is another VGAM1678 host target gene. KIAA1727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1727 BINDING SITE, designated SEQ ID:32033, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56711] Another function of VGAM1678 is therefore inhibition of KIAA1727 (Accession XM\_034262). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1727. MGC4415 (Accession NM\_031484) is another VGAM1678 host target gene. MGC4415 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4415 BINDING SITE, designated SEQ ID:25570, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56712] Another function of VGAM1678 is therefore inhibition of MGC4415 (Accession NM\_031484). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4415. Netrin 4 (NTN4, Accession XM\_031896) is another VGAM1678 host target gene. NTN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NTN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTN4 BINDING SITE, designated SEQ ID:31513, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56713] Another function of VGAM1678 is therefore inhibition of

Netrin 4 (NTN4, Accession XM\_031896). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTN4. RNA-binding Region (RNP1, RRM) Containing 1 (RNPC1, Accession NM\_017495) is another VGAM1678 host target gene. RNPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNPC1 BINDING SITE, designated SEQ ID:18958, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56714] Another function of VGAM1678 is therefore inhibition of RNA-binding Region (RNP1, RRM) Containing 1 (RNPC1, Accession NM\_017495). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNPC1. Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM\_037202) is another VGAM1678 host target gene. SS18L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by SS18L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SS18L1 BINDING SITE, designated SEQ ID:32562, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56715] Another function of VGAM1678 is therefore inhibition of Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM\_037202). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SS18L1. LOC114932 (Accession XM\_052614) is another VGAM1678 host target gene. LOC114932 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC114932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114932 BINDING SITE, designated SEQ ID:36005, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56716] Another function of VGAM1678 is therefore inhibition of

LOC114932 (Accession XM\_052614). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114932. LOC145497 (Accession XM\_085150) is another VGAM1678 host target gene. LOC145497 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145497 BINDING SITE, designated SEQ ID:37871, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56717] Another function of VGAM1678 is therefore inhibition of LOC145497 (Accession XM\_085150). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145497. LOC145978 (Accession XM\_085288) is another VGAM1678 host target gene. LOC145978 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145978, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC145978 BINDING SITE, designated SEQ ID:38033, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56718] Another function of VGAM1678 is therefore inhibition of LOC145978 (Accession XM\_085288). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145978. LOC146429 (Accession XM\_096998) is another VGAM1678 host target gene. LOC146429 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146429 BINDING SITE, designated SEQ ID:40696, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56719] Another function of VGAM1678 is therefore inhibition of LOC146429 (Accession XM\_096998). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146429. LOC149386 (Accession XM\_097631) is an-

other VGAM1678 host target gene. LOC149386 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149386 BINDING SITE, designated SEQ ID:40987, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56720] Another function of VGAM1678 is therefore inhibition of LOC149386 (Accession XM\_097631). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149386. LOC158581 (Accession XM\_098968) is another VGAM1678 host target gene. LOC158581 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158581, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158581 BINDING SITE, designated SEQ ID:42015, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.



[56721] Another function of VGAM1678 is therefore inhibition of LOC158581 (Accession XM\_098968). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158581. LOC202460 (Accession XM\_114493) is another VGAM1678 host target gene. LOC202460 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202460 BINDING SITE, designated SEQ ID:42984, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56722] Another function of VGAM1678 is therefore inhibition of LOC202460 (Accession XM\_114493). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202460. LOC219894 (Accession XM\_167782) is another VGAM1678 host target gene. LOC219894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219894, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219894 BINDING SITE, designated SEQ ID:44792, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56723] Another function of VGAM1678 is therefore inhibition of LOC219894 (Accession XM\_167782). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219894. LOC221751 (Accession XM\_166370) is another VGAM1678 host target gene. LOC221751 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221751, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221751 BINDING SITE, designated SEQ ID:44190, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56724] Another function of VGAM1678 is therefore inhibition of LOC221751 (Accession XM\_166370). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221751. LOC254268 (Accession XM\_170913) is another VGAM1678 host target gene. LOC254268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254268 BINDING SITE, designated SEQ ID:45691, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56725] Another function of VGAM1678 is therefore inhibition of LOC254268 (Accession XM\_170913). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254268. LOC255252 (Accession XM\_170779) is another VGAM1678 host target gene. LOC255252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255252 BINDING SITE, designated SEQ ID:45546, to the nucleotide sequence of VGAM1678 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4389.

[56726] Another function of VGAM1678 is therefore inhibition of LOC255252 (Accession XM\_170779). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255252. LOC90499 (Accession XM\_032170) is another VGAM1678 host target gene. LOC90499 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90499 BINDING SITE, designated SEQ ID:31581, to the nucleotide sequence of VGAM1678 RNA, herein designated VGAM RNA, also designated SEQ ID:4389.

[56727] Another function of VGAM1678 is therefore inhibition of LOC90499 (Accession XM\_032170). Accordingly, utilities of VGAM1678 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90499. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1679 (VGAM1679) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56728] VGAM1679 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1679 was detected is described hereinabove with reference to Figs. 1–8.

[56729] VGAM1679 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Viral Hemorrhagic Septicemia Virus. VGAM1679 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56730] VGAM1679 gene encodes a VGAM1679 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1679 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1679 precursor RNA is designated SEQ ID:1665, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1665 is located at position 1372 relative to the genome of Viral Hemorrhagic Septicemia Virus.

[56731] VGAM1679 precursor RNA folds onto itself, forming

VGAM1679 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56732] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1679 folded precursor RNA into VGAM1679 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1679 RNA is designated SEQ ID:4390, and is provided hereinbelow with reference to the sequence listing part.

[56733] VGAM1679 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1679 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1679 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56734] VGAM1679 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1679 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1679 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1679 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1679 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56735] The complementary binding of VGAM1679 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1679 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1679 host target RNA into VGAM1679 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56736] It is appreciated that VGAM1679 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1679 host target genes. The mRNA of each one of this plurality of VGAM1679 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1679 RNA, herein designated VGAM RNA, and which when bound by VGAM1679 RNA causes inhibition of translation of respective one or more VGAM1679 host target proteins.

[56737] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with



specific reference to translational inhibition exerted by VGAM1679 gene, herein designated VGAM GENE, on one or more VGAM1679 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56738] It is yet further appreciated that a function of VGAM1679 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of viral infection by Viral Hemorrhagic Septicemia Virus. Specific functions, and accordingly utilities, of VGAM1679 correlate with, and may be deduced from, the identity of the host target genes which VGAM1679

binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56739] Nucleotide sequences of the VGAM1679 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1679 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1679 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1679 are further described hereinbelow with reference to Table 1.

[56740] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1679 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1679 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56741] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1679 gene, herein designated VGAM is inhibition of expression of VGAM1679 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1679 correlate with, and may be deduced from, the identity of the target genes which VGAM1679 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[56742] Cyclin-dependent Kinase 5, Regulatory Subunit 2 (p39) (CDK5R2, Accession NM\_003936) is a VGAM1679 host target gene. CDK5R2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDK5R2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK5R2 BINDING SITE, designated SEQ ID:10042, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56743] A function of VGAM1679 is therefore inhibition of Cyclin-dependent Kinase 5, Regulatory Subunit 2 (p39) (CDK5R2, Accession NM\_003936), a gene which acts as a regulatory subunit for the cyclin-dependent CDK5. Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK5R2. The function of CDK5R2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM403. Paired Basic Amino Acid Cleaving System 4 (PACE4, Accession NM\_138319) is an-

other VGAM1679 host target gene. PACE4 BINDING SITE1 and PACE4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PACE4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACE4 BINDING SITE1 and PACE4 BINDING SITE2, designated SEQ ID:28720 and SEQ ID:8431 respectively, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56744] Another function of VGAM1679 is therefore inhibition of Paired Basic Amino Acid Cleaving System 4 (PACE4, Accession NM\_138319), a gene which processes hormone precursors by cleaving paired basic amino acids. Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACE4. The function of PACE4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1194.ARL8 (Accession XM\_167671) is another VGAM1679 host target gene. ARL8 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by ARL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARL8 BINDING SITE, designated SEQ ID:44763, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56745] Another function of VGAM1679 is therefore inhibition of ARL8 (Accession XM\_167671). Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARL8. FLJ13659 (Accession NM\_025189) is another VGAM1679 host target gene. FLJ13659 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13659, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13659 BINDING SITE, designated SEQ ID:24830, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56746] Another function of VGAM1679 is therefore inhibition of FLJ13659 (Accession NM\_025189). Accordingly, utilities of

VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13659. Guanine Nucleotide Binding Protein (G protein), Gamma 4 (GNG4, Accession NM\_004485) is another VGAM1679 host target gene. GNG4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GNG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNG4 BINDING SITE, designated SEQ ID:10811, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56747] Another function of VGAM1679 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Gamma 4 (GNG4, Accession NM\_004485). Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNG4. HTCD37 (Accession XM\_041884) is another VGAM1679 host target gene. HTCD37 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HTCD37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTCD37 BINDING SITE, designated SEQ ID:33620, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56748] Another function of VGAM1679 is therefore inhibition of HTCD37 (Accession XM\_041884). Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTCD37. KIAA0451 (Accession NM\_014826) is another VGAM1679 host target gene. KIAA0451 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0451 BINDING SITE, designated SEQ ID:16803, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56749] Another function of VGAM1679 is therefore inhibition of KIAA0451 (Accession NM\_014826). Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0451. MGC2562 (Accession NM\_032374) is another VGAM1679 host target gene. MGC2562 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC2562, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2562 BINDING SITE, designated SEQ ID:26163, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56750] Another function of VGAM1679 is therefore inhibition of MGC2562 (Accession NM\_032374). Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2562. Transducer of ERBB2, 2 (TOB2, Accession XM\_170995) is another VGAM1679 host target gene. TOB2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TOB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOB2 BINDING SITE, designated SEQ ID:45770, to the nucleotide sequence of VGAM1679 RNA, herein



designated VGAM RNA, also designated SEQ ID:4390.

[56751] Another function of VGAM1679 is therefore inhibition of Transducer of ERBB2, 2 (TOB2, Accession XM\_170995). Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOB2. LOC149576 (Accession XM\_086580) is another VGAM1679 host target gene. LOC149576 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149576 BINDING SITE, designated SEQ ID:38775, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56752] Another function of VGAM1679 is therefore inhibition of LOC149576 (Accession XM\_086580). Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149576. LOC151278 (Accession XM\_087156) is another VGAM1679 host target gene. LOC151278 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC151278, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151278 BINDING SITE, designated SEQ ID:39097, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56753] Another function of VGAM1679 is therefore inhibition of LOC151278 (Accession XM\_087156). Accordingly, utilities of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151278. LOC91565 (Accession XM\_039231) is another VGAM1679 host target gene. LOC91565 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91565 BINDING SITE, designated SEQ ID:33024, to the nucleotide sequence of VGAM1679 RNA, herein designated VGAM RNA, also designated SEQ ID:4390.

[56754] Another function of VGAM1679 is therefore inhibition of LOC91565 (Accession XM\_039231). Accordingly, utilities

of VGAM1679 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91565. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1680 (VGAM1680) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56755] VGAM1680 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1680 was detected is described hereinabove with reference to Figs. 1-8.

[56756] VGAM1680 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Viral Hemorrhagic Septicemia Virus. VGAM1680 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56757] VGAM1680 gene encodes a VGAM1680 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1680 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1680 precursor RNA is designated SEQ ID:1666, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1666 is located at position 10244 relative to the genome of Viral Hemorrhagic Septicemia Virus.

[56758] VGAM1680 precursor RNA folds onto itself, forming VGAM1680 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56759] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1680 folded precursor RNA into VGAM1680 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1680 RNA is designated SEQ ID:4391, and

is provided hereinbelow with reference to the sequence listing part.

[56760] VGAM1680 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1680 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1680 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[56761] VGAM1680 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1680 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1680 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1680 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1680 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56762] The complementary binding of VGAM1680 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1680 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1680 host target RNA into VGAM1680 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56763] It is appreciated that VGAM1680 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1680 host target genes. The mRNA of each one of this plurality of VGAM1680 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1680 RNA, herein designated VGAM RNA, and which when bound by VGAM1680 RNA causes inhibition of translation of respective one or more VGAM1680 host target proteins.

[56764] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1680 gene, herein designated VGAM GENE, on one or more VGAM1680 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56765] It is yet further appreciated that a function of VGAM1680 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1680 include diagnosis, prevention and treatment of viral infection by Viral Hemorrhagic Septicemia Virus. Specific functions, and accordingly utilities, of VGAM1680 correlate with, and may be deduced from, the identity of the host target genes which VGAM1680 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56766] Nucleotide sequences of the VGAM1680 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1680 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1680 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1680 are further described hereinbelow with reference to Table 1.

[56767] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1680 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1680 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56768] As mentioned hereinabove with reference to Fig. 1, a



function of VGAM1680 gene, herein designated VGAM is inhibition of expression of VGAM1680 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1680 correlate with, and may be deduced from, the identity of the target genes which VGAM1680 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56769] Collagen, Type XIII, Alpha 1 (COL13A1, Accession NM\_080799) is a VGAM1680 host target gene. COL13A1 BINDING SITE1 through COL13A1 BINDING SITE7 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL13A1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL13A1 BINDING SITE1 through COL13A1 BINDING SITE7, designated SEQ ID:28066, SEQ ID:28068, SEQ ID:28070, SEQ ID:28072, SEQ ID:28074, SEQ ID:28076 and SEQ ID:11703 respectively, to the nucleotide sequence of VGAM1680 RNA, herein designated VGAM RNA, also designated SEQ ID:4391.

[56770] A function of VGAM1680 is therefore inhibition of Collagen, Type XIII, Alpha 1 (COL13A1, Accession NM\_080799),

a gene which is specific for basement membranes. Accordingly, utilities of VGAM1680 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL13A1. The function of COL13A1 has been established by previous studies. Tikka et al. (1988) isolated and partially characterized the gene for the alpha-1 chain of type XIII collagen. Some of the features resembled those of genes for fibrillar collagens, but other features were distinctly different. Analysis of overlapping cDNA clones and nuclease S1 mapping of mRNAs indicated 1 alternative splicing site causing a deletion of 36 bp from the mature mRNA. The 36 bp represented a single exon. Furthermore, a 45-bp exon was also subject to alternative splicing. Of the 3 major groups of collagens--the fibrillar collagens, the large nonfibrillar collagens, and the short-chain collagens--type XIII collagen belongs to the third group. Shows et al. (1989) mapped the COL13A1 gene to 10q22 by a combination of somatic cell hybrid study and in situ hybridization. Pajunen et al. (1989) assigned the COL13A1 gene to 10q11-qter by Southern blot hybridization of DNA from human/rodent somatic cell hybrids. The gene for type XIII collagen (COL13A1) and that for the alpha-1 subunit of prolyl

4-hydroxylase (P4HA1; 176710) had been assigned to 10q22 and 10q21.3–q23.1 by isotopic in situ hybridization. Horelli-Kuitunen et al. (1997) applied fluorescence in situ hybridization (FISH) combined with targets representing different levels of resolution to determine the order of these genes along chromosome 10, their transcriptional orientation, and the distance between them. Using mechanically stretched chromosomes they determined the order to be cen–COL13A1–P4HA1–tel. By combining the data from stretched chromosomes and interphase nuclei, they found that the transcriptional orientation was tail-to-tail. The distance between the genes was measured by fiber FISH to be approximately 550 kb.

[56771] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[56772] Tikka, L.; Pihlajaniemi, T.; Henttu, P.; Prockop, D. J.; Trygvason, K. : Gene structure for the alpha-1 chain of a human short-chain collagen (type XIII) with alternatively spliced transcripts and translation termination codon at the 5-prime end of the last exon. Proc. Nat. Acad. Sci. 85: 7491–7495, 1988. ; and

[56773] Horelli-Kuitunen, N.; Kvist, A.-P.; Helaakoski, T.; Kivirikko,

K.; Pihlajaniemi, T.; Palotie, A. : The order and transcriptional orientation of the human COL13A1 and P4HA genes on chrom.

[56774] Further studies establishing the function and utilities of COL13A1 are found in John Hopkins OMIM database record ID 120350, and in cited publications numbered 12045–12048 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hippocalcin-like 1 (HPCAL1, Accession NM\_002149) is another VGAM1680 host target gene. HPCAL1 BINDING SITE1 and HPCAL1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HPCAL1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPCAL1 BINDING SITE1 and HPCAL1 BINDING SITE2, designated SEQ ID:7931 and SEQ ID:36465 respectively, to the nucleotide sequence of VGAM1680 RNA, herein designated VGAM RNA, also designated SEQ ID:4391.

[56775] Another function of VGAM1680 is therefore inhibition of Hippocalcin-like 1 (HPCAL1, Accession NM\_002149). Accordingly, utilities of VGAM1680 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with HPCAL1. KIAA1910 (Accession XM\_055514) is another VGAM1680 host target gene. KIAA1910 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1910 BINDING SITE, designated SEQ ID:36285, to the nucleotide sequence of VGAM1680 RNA, herein designated VGAM RNA, also designated SEQ ID:4391.

[56776] Another function of VGAM1680 is therefore inhibition of KIAA1910 (Accession XM\_055514). Accordingly, utilities of VGAM1680 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1910. MGC10818 (Accession NM\_030568) is another VGAM1680 host target gene. MGC10818 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC10818, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC10818 BINDING SITE, designated SEQ ID:24940, to the nucleotide sequence of VGAM1680 RNA, herein designated VGAM RNA, also designated SEQ ID:4391.

[56777] Another function of VGAM1680 is therefore inhibition of MGC10818 (Accession NM\_030568). Accordingly, utilities of VGAM1680 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10818. RAB40C, Member RAS Oncogene Family (RAB40C, Accession NM\_021168) is another VGAM1680 host target gene. RAB40C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB40C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB40C BINDING SITE, designated SEQ ID:22145, to the nucleotide sequence of VGAM1680 RNA, herein designated VGAM RNA, also designated SEQ ID:4391.

[56778] Another function of VGAM1680 is therefore inhibition of RAB40C, Member RAS Oncogene Family (RAB40C, Accession NM\_021168). Accordingly, utilities of VGAM1680 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB40C. SCAMP-4

(Accession NM\_079834) is another VGAM1680 host target gene. SCAMP-4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCAMP-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAMP-4 BINDING SITE, designated SEQ ID:27822, to the nucleotide sequence of VGAM1680 RNA, herein designated VGAM RNA, also designated SEQ ID:4391.

[56779] Another function of VGAM1680 is therefore inhibition of SCAMP-4 (Accession NM\_079834). Accordingly, utilities of VGAM1680 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCAMP-4. LOC221288 (Accession XM\_168058) is another VGAM1680 host target gene. LOC221288 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221288, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221288 BINDING SITE, designated SEQ ID:44969, to the nucleotide sequence of VGAM1680 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4391.

[56780] Another function of VGAM1680 is therefore inhibition of LOC221288 (Accession XM\_168058). Accordingly, utilities of VGAM1680 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221288. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1681 (VGAM1681) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56781] VGAM1681 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1681 was detected is described hereinabove with reference to Figs. 1–8.

[56782] VGAM1681 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vesicular Stomatitis Indiana Virus. VGAM1681 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56783] VGAM1681 gene encodes a VGAM1681 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other



miRNA genes, and unlike most ordinary genes, VGAM1681 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1681 precursor RNA is designated SEQ ID:1667, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1667 is located at position 3549 relative to the genome of Vesicular Stomatitis Indiana Virus.

[56784] VGAM1681 precursor RNA folds onto itself, forming VGAM1681 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56785] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1681 folded precursor RNA into VGAM1681 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1681 RNA is designated SEQ ID:4392, and is provided hereinbelow with reference to the sequence listing part.

[56786] VGAM1681 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1681 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1681 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56787] VGAM1681 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1681 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1681 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1681 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1681 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56788] The complementary binding of VGAM1681 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1681 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1681 host target RNA into VGAM1681 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56789] It is appreciated that VGAM1681 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1681 host target genes. The mRNA of

each one of this plurality of VGAM1681 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1681 RNA, herein designated VGAM RNA, and which when bound by VGAM1681 RNA causes inhibition of translation of respective one or more VGAM1681 host target proteins.

[56790] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1681 gene, herein designated VGAM GENE, on one or more VGAM1681 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[56791] It is yet further appreciated that a function of VGAM1681 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1681 include diagnosis, prevention and treatment of viral infection by Vesicular Stomatitis Indiana Virus. Specific functions, and accordingly utilities, of VGAM1681 correlate with, and may be deduced from, the identity of the host target genes which VGAM1681 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56792] Nucleotide sequences of the VGAM1681 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1681 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1681 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1681 are further described hereinbelow with reference to Table 1.

[56793] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1681 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1681 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56794] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1681 gene, herein designated VGAM is inhibition of expression of VGAM1681 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1681 correlate with, and may be deduced from, the identity of the target genes which VGAM1681 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56795] Cystic Fibrosis Transmembrane Conductance Regulator, ATP-binding Cassette (sub-family C, member 7) (CFTR, Accession NM\_000492) is a VGAM1681 host target gene. CFTR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CFTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CFTR BINDING SITE, designated SEQ ID:6103, to the nucleotide sequence of VGAM1681 RNA, herein designated VGAM RNA, also designated SEQ ID:4392.

[56796] A function of VGAM1681 is therefore inhibition of Cystic Fibrosis Transmembrane Conductance Regulator, ATP-

binding Cassette (sub-family C, member 7) (CFTR, Accession NM\_000492). Accordingly, utilities of VGAM1681 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CFTR. Steroid Sulfatase (microsomal), Arylsulfatase C, Isozyme S (STS, Accession NM\_000351) is another VGAM1681 host target gene. STS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STS BINDING SITE, designated SEQ ID:5911, to the nucleotide sequence of VGAM1681 RNA, herein designated VGAM RNA, also designated SEQ ID:4392.

[56797] Another function of VGAM1681 is therefore inhibition of Steroid Sulfatase (microsomal), Arylsulfatase C, Isozyme S (STS, Accession NM\_000351). Accordingly, utilities of VGAM1681 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STS. FLJ11286 (Accession NM\_018381) is another VGAM1681 host target gene. FLJ11286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11286, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11286 BINDING SITE, designated SEQ ID:20414, to the nucleotide sequence of VGAM1681 RNA, herein designated VGAM RNA, also designated SEQ ID:4392.

[56798] Another function of VGAM1681 is therefore inhibition of FLJ11286 (Accession NM\_018381). Accordingly, utilities of VGAM1681 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11286. KIAA0747 (Accession NM\_015292) is another VGAM1681 host target gene. KIAA0747 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0747, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0747 BINDING SITE, designated SEQ ID:17612, to the nucleotide sequence of VGAM1681 RNA, herein designated VGAM RNA, also designated SEQ ID:4392.

[56799] Another function of VGAM1681 is therefore inhibition of KIAA0747 (Accession NM\_015292). Accordingly, utilities of VGAM1681 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with KIAA0747. MGC13061 (Accession NM\_032322) is another VGAM1681 host target gene. MGC13061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13061 BINDING SITE, designated SEQ ID:26132, to the nucleotide sequence of VGAM1681 RNA, herein designated VGAM RNA, also designated SEQ ID:4392.

[56800] Another function of VGAM1681 is therefore inhibition of MGC13061 (Accession NM\_032322). Accordingly, utilities of VGAM1681 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13061. Talin 2 (TLN2, Accession XM\_029473) is another VGAM1681 host target gene. TLN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLN2 BINDING SITE, designated SEQ ID:30897, to the nucleotide se-

quence of VGAM1681 RNA, herein designated VGAM RNA, also designated SEQ ID:4392.

[56801] Another function of VGAM1681 is therefore inhibition of Talin 2 (TLN2, Accession XM\_029473). Accordingly, utilities of VGAM1681 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLN2. LOC151361 (Accession XM\_098048) is another VGAM1681 host target gene. LOC151361 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151361 BINDING SITE, designated SEQ ID:41334, to the nucleotide sequence of VGAM1681 RNA, herein designated VGAM RNA, also designated SEQ ID:4392.

[56802] Another function of VGAM1681 is therefore inhibition of LOC151361 (Accession XM\_098048). Accordingly, utilities of VGAM1681 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151361. LOC158314 (Accession XM\_098920) is another VGAM1681 host target gene. LOC158314 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC158314, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158314 BINDING SITE, designated SEQ ID:41952, to the nucleotide sequence of VGAM1681 RNA, herein designated VGAM RNA, also designated SEQ ID:4392.

[56803] Another function of VGAM1681 is therefore inhibition of LOC158314 (Accession XM\_098920). Accordingly, utilities of VGAM1681 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158314. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1682 (VGAM1682) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56804] VGAM1682 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1682 was detected is described hereinabove with reference to Figs. 1-8.

[56805] VGAM1682 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Vesicular Stomatitis Indiana Virus. VGAM1682 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56806] VGAM1682 gene encodes a VGAM1682 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1682 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1682 precursor RNA is designated SEQ ID:1668, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1668 is located at position 10245 relative to the genome of Vesicular Stomatitis Indiana Virus.

[56807] VGAM1682 precursor RNA folds onto itself, forming VGAM1682 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56808] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1682 folded precursor RNA into VGAM1682 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1682 RNA is designated SEQ ID:4393, and is provided hereinbelow with reference to the sequence listing part.

[56809] VGAM1682 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1682 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1682 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56810] VGAM1682 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1682 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1682 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1682 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1682 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56811] The complementary binding of VGAM1682 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1682 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1682

host target RNA into VGAM1682 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56812] It is appreciated that VGAM1682 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1682 host target genes. The mRNA of each one of this plurality of VGAM1682 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1682 RNA, herein designated VGAM RNA, and which when bound by VGAM1682 RNA causes inhibition of translation of respective one or more VGAM1682 host target proteins.

[56813] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1682 gene, herein designated VGAM GENE, on one or more VGAM1682 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56814] It is yet further appreciated that a function of VGAM1682 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of viral infection by Vesicular Stomatitis Indiana Virus. Specific functions, and accordingly utilities, of VGAM1682 correlate with, and may be deduced from, the identity of the host target genes which VGAM1682 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56815] Nucleotide sequences of the VGAM1682 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1682 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1682 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1682 are further



described hereinbelow with reference to Table 1.

[56816] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1682 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1682 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56817] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1682 gene, herein designated VGAM is inhibition of expression of VGAM1682 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1682 correlate with, and may be deduced from, the identity of the target genes which VGAM1682 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56818] UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 3 (B3GALT3, Accession NM\_003781) is a VGAM1682 host target gene. B3GALT3 BINDING SITE1 through B3GALT3 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GALT3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT3 BINDING SITE1 through B3GALT3 BINDING SITE3, designated SEQ ID:9867, SEQ ID:27016 and SEQ ID:27019 respectively, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56819] A function of VGAM1682 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 3 (B3GALT3, Accession NM\_003781). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT3. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 28 (DDX28, Accession NM\_018380) is another VGAM1682 host target gene. DDX28 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DDX28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX28 BINDING SITE, designated SEQ ID:20406, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56820] Another function of VGAM1682 is therefore inhibition of

DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 28 (DDX28, Accession NM\_018380). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX28. KIAA1323 (Accession XM\_032146) is another VGAM1682 host target gene. KIAA1323 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1323 BINDING SITE, designated SEQ ID:31572, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56821] Another function of VGAM1682 is therefore inhibition of KIAA1323 (Accession XM\_032146). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1323. MGC5306 (Accession NM\_024116) is another VGAM1682 host target gene. MGC5306 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC5306, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5306 BINDING SITE, designated SEQ ID:23570, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56822] Another function of VGAM1682 is therefore inhibition of MGC5306 (Accession NM\_024116). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5306. PRO1386 (Accession NM\_031269) is another VGAM1682 host target gene. PRO1386 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1386 BINDING SITE, designated SEQ ID:25292, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56823] Another function of VGAM1682 is therefore inhibition of PRO1386 (Accession NM\_031269). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PRO1386. Testis-specific Transcript, Y-linked 9 (TTY9, Accession NM\_031927) is another VGAM1682 host target gene. TTY9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TTY9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTY9 BINDING SITE, designated SEQ ID:25681, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56824] Another function of VGAM1682 is therefore inhibition of Testis-specific Transcript, Y-linked 9 (TTY9, Accession NM\_031927). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTY9. LOC143286 (Accession XM\_096412) is another VGAM1682 host target gene. LOC143286 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143286 BINDING SITE, desig-

nated SEQ ID:40351, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56825] Another function of VGAM1682 is therefore inhibition of LOC143286 (Accession XM\_096412). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143286. LOC150519 (Accession XM\_086937) is another VGAM1682 host target gene. LOC150519 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150519, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150519 BINDING SITE, designated SEQ ID:38989, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56826] Another function of VGAM1682 is therefore inhibition of LOC150519 (Accession XM\_086937). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150519. LOC222128 (Accession XM\_166560) is another VGAM1682 host target gene. LOC222128 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC222128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222128 BINDING SITE, designated SEQ ID:44543, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56827] Another function of VGAM1682 is therefore inhibition of LOC222128 (Accession XM\_166560). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222128. LOC57795 (Accession XM\_045110) is another VGAM1682 host target gene. LOC57795 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC57795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57795 BINDING SITE, designated SEQ ID:34360, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56828] Another function of VGAM1682 is therefore inhibition of

LOC57795 (Accession XM\_045110). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57795. LOC85479 (Accession NM\_033105) is another VGAM1682 host target gene. LOC85479 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC85479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC85479 BINDING SITE, designated SEQ ID:26959, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56829] Another function of VGAM1682 is therefore inhibition of LOC85479 (Accession NM\_033105). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC85479. LOC92573 (Accession XM\_045884) is another VGAM1682 host target gene. LOC92573 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the



complementarity of the nucleotide sequences of LOC92573 BINDING SITE, designated SEQ ID:34602, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56830] Another function of VGAM1682 is therefore inhibition of LOC92573 (Accession XM\_045884). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92573. LOC92973 (Accession XM\_048529) is another VGAM1682 host target gene. LOC92973 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92973, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92973 BINDING SITE, designated SEQ ID:35182, to the nucleotide sequence of VGAM1682 RNA, herein designated VGAM RNA, also designated SEQ ID:4393.

[56831] Another function of VGAM1682 is therefore inhibition of LOC92973 (Accession XM\_048529). Accordingly, utilities of VGAM1682 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92973. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1683 (VGAM1683) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56832] VGAM1683 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1683 was detected is described hereinabove with reference to Figs. 1–8.

[56833] VGAM1683 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vesicular Stomatitis Indiana Virus. VGAM1683 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56834] VGAM1683 gene encodes a VGAM1683 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1683 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1683 precursor RNA is designated SEQ ID:1669, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1669 is located at position 8817 relative to the genome of Vesicular Stomatitis Indiana Virus.

[56835] VGAM1683 precursor RNA folds onto itself, forming VGAM1683 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56836] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1683 folded precursor RNA into VGAM1683 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1683 RNA is designated SEQ ID:4394, and is provided hereinbelow with reference to the sequence listing part.

[56837] VGAM1683 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1683 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1683 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56838] VGAM1683 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1683 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1683 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1683 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1683 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[56839] The complementary binding of VGAM1683 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1683 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1683 host target RNA into VGAM1683 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56840] It is appreciated that VGAM1683 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1683 host target genes. The mRNA of each one of this plurality of VGAM1683 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1683 RNA, herein designated VGAM RNA, and which when bound by VGAM1683 RNA causes inhibition of translation of respective one or more

VGAM1683 host target proteins.

[56841] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1683 gene, herein designated VGAM GENE, on one or more VGAM1683 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56842] It is yet further appreciated that a function of VGAM1683 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of viral infection by Vesicular Stomatitis Indiana

Virus. Specific functions, and accordingly utilities, of VGAM1683 correlate with, and may be deduced from, the identity of the host target genes which VGAM1683 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56843] Nucleotide sequences of the VGAM1683 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1683 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1683 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1683 are further described hereinbelow with reference to Table 1.

[56844] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1683 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1683 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56845] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1683 gene, herein designated VGAM is inhibition of expression of VGAM1683 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1683 correlate with, and may be deduced from, the identity of the target genes which VGAM1683 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56846] Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM\_042963) is a VGAM1683 host target gene. ARHGEF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF6 BINDING SITE, designated SEQ ID:33849, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56847] A function of VGAM1683 is therefore inhibition of Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM\_042963). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF6. BIG1 (Accession NM\_006421) is another VGAM1683 host target gene. BIG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region



of mRNA encoded by BIG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIG1 BINDING SITE, designated SEQ ID:13137, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56848] Another function of VGAM1683 is therefore inhibition of BIG1 (Accession NM\_006421), a gene which is a guanine nucleotide-exchange protein, has a role in vesicular transport. Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIG1. The function of BIG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1190. V-raf-1 Murine Leukemia Viral Oncogene Homolog 1 (RAF1, Accession XM\_087425) is another VGAM1683 host target gene. RAF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of RAF1 BINDING SITE, designated SEQ ID:39246, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56849] Another function of VGAM1683 is therefore inhibition of V-raf-1 Murine Leukemia Viral Oncogene Homolog 1 (RAF1, Accession XM\_087425). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAF1. Sal-like 2 (Drosophila) (SALL2, Accession XM\_033473) is another VGAM1683 host target gene. SALL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SALL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SALL2 BINDING SITE, designated SEQ ID:31938, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56850] Another function of VGAM1683 is therefore inhibition of Sal-like 2 (Drosophila) (SALL2, Accession XM\_033473). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SALL2. Cysteine and Tyrosine-rich 1

(CYR1, Accession NM\_052954) is another VGAM1683 host target gene. CYR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYR1 BINDING SITE, designated SEQ ID:27516, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56851] Another function of VGAM1683 is therefore inhibition of Cysteine and Tyrosine-rich 1 (CYR1, Accession NM\_052954). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYR1. FLJ13782 (Accession NM\_024915) is another VGAM1683 host target gene. FLJ13782 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13782 BINDING SITE, designated SEQ ID:24439, to the nucleotide sequence of VGAM1683

RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56852] Another function of VGAM1683 is therefore inhibition of FLJ13782 (Accession NM\_024915). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13782. KIAA0895 (Accession XM\_166573) is another VGAM1683 host target gene. KIAA0895 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0895 BINDING SITE, designated SEQ ID:44547, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56853] Another function of VGAM1683 is therefore inhibition of KIAA0895 (Accession XM\_166573). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0895. KIAA1255 (Accession XM\_040626) is another VGAM1683 host target gene. KIAA1255 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1255, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1255 BINDING SITE, designated SEQ ID:33346, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56854] Another function of VGAM1683 is therefore inhibition of KIAA1255 (Accession XM\_040626). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1255. KIAA1387 (Accession XM\_048092) is another VGAM1683 host target gene. KIAA1387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1387 BINDING SITE, designated SEQ ID:35105, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56855] Another function of VGAM1683 is therefore inhibition of KIAA1387 (Accession XM\_048092). Accordingly, utilities

of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1387. SCYB10 (Accession NM\_001565) is another VGAM1683 host target gene. SCYB10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCYB10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYB10 BINDING SITE, designated SEQ ID:7293, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56856] Another function of VGAM1683 is therefore inhibition of SCYB10 (Accession NM\_001565). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCYB10. Solute Carrier Family 1 (glutamate transporter), Member 7 (SLC1A7, Accession NM\_006671) is another VGAM1683 host target gene. SLC1A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of SLC1A7 BINDING SITE, designated SEQ ID:13490, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56857] Another function of VGAM1683 is therefore inhibition of Solute Carrier Family 1 (glutamate transporter), Member 7 (SLC1A7, Accession NM\_006671). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A7. LOC203339 (Accession XM\_117534) is another VGAM1683 host target gene. LOC203339 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203339, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203339 BINDING SITE, designated SEQ ID:43527, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56858] Another function of VGAM1683 is therefore inhibition of LOC203339 (Accession XM\_117534). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC203339. LOC222234 (Accession XM\_168558) is another VGAM1683 host target gene. LOC222234 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222234, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222234 BINDING SITE, designated SEQ ID:45239, to the nucleotide sequence of VGAM1683 RNA, herein designated VGAM RNA, also designated SEQ ID:4394.

[56859] Another function of VGAM1683 is therefore inhibition of LOC222234 (Accession XM\_168558). Accordingly, utilities of VGAM1683 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222234. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1684 (VGAM1684) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56860] VGAM1684 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.



The method by which VGAM1684 was detected is described hereinabove with reference to Figs. 1–8.

[56861] VGAM1684 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vesicular Stomatitis Indiana Virus. VGAM1684 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56862] VGAM1684 gene encodes a VGAM1684 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1684 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1684 precursor RNA is designated SEQ ID:1670, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1670 is located at position 5581 relative to the genome of Vesicular Stomatitis Indiana Virus.

[56863] VGAM1684 precursor RNA folds onto itself, forming VGAM1684 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56864] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1684 folded precursor RNA into VGAM1684 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 68%) nucleotide sequence of VGAM1684 RNA is designated SEQ ID:4395, and is provided hereinbelow with reference to the sequence listing part.

[56865] VGAM1684 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1684 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1684 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56866] VGAM1684 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1684 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1684 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1684 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1684 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[56867] The complementary binding of VGAM1684 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1684 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1684 host target RNA into VGAM1684 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56868] It is appreciated that VGAM1684 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1684 host target genes. The mRNA of each one of this plurality of VGAM1684 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1684 RNA, herein designated VGAM RNA, and which when bound by VGAM1684 RNA causes inhibition of translation of respective one or more VGAM1684 host target proteins.

[56869] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1684 gene, herein designated VGAM GENE, on one or more VGAM1684 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56870] It is yet further appreciated that a function of VGAM1684 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1684 include diagnosis, prevention and treatment of viral infection by Vesicular Stomatitis Indiana Virus. Specific functions, and accordingly utilities, of VGAM1684 correlate with, and may be deduced from, the identity of the host target genes which VGAM1684 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56871] Nucleotide sequences of the VGAM1684 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1684 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1684 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1684 are further described hereinbelow with reference to Table 1.

[56872] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1684 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1684 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56873] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1684 gene, herein designated VGAM is inhibition of expression of VGAM1684 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1684 correlate with, and may be deduced from, the identity of the target genes which VGAM1684 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56874] Sorting Nexin 3 (SNX3, Accession NM\_003795) is a VGAM1684 host target gene. SNX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNX3, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX3 BINDING SITE, designated SEQ ID:9876, to the nucleotide sequence of VGAM1684 RNA, herein designated VGAM RNA, also designated SEQ ID:4395.

[56875] A function of VGAM1684 is therefore inhibition of Sorting Nexin 3 (SNX3, Accession NM\_003795). Accordingly, utilities of VGAM1684 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX3. LOC115265 (Accession XM\_055596) is another VGAM1684 host target gene. LOC115265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115265 BINDING SITE, designated SEQ ID:36305, to the nucleotide sequence of VGAM1684 RNA, herein designated VGAM RNA, also designated SEQ ID:4395.

[56876] Another function of VGAM1684 is therefore inhibition of LOC115265 (Accession XM\_055596). Accordingly, utilities of VGAM1684 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC115265. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1685 (VGAM1685) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56877] VGAM1685 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1685 was detected is described hereinabove with reference to Figs. 1–8.

[56878] VGAM1685 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vesicular Stomatitis Indiana Virus. VGAM1685 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56879] VGAM1685 gene encodes a VGAM1685 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1685 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1685 precursor RNA is desig-



nated SEQ ID:1671, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1671 is located at position 4965 relative to the genome of Vesicular Stomatitis Indiana Virus.

- [56880] VGAM1685 precursor RNA folds onto itself, forming VGAM1685 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [56881] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1685 folded precursor RNA into VGAM1685 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM1685 RNA is designated SEQ ID:4396, and is provided hereinbelow with reference to the sequence

listing part.

[56882] VGAM1685 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1685 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1685 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56883] VGAM1685 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1685 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1685 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1685 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1685 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56884] The complementary binding of VGAM1685 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1685 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1685 host target RNA into VGAM1685 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56885] It is appreciated that VGAM1685 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1685 host target genes. The mRNA of each one of this plurality of VGAM1685 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1685 RNA, herein designated VGAM

RNA, and which when bound by VGAM1685 RNA causes inhibition of translation of respective one or more VGAM1685 host target proteins.

[56886] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1685 gene, herein designated VGAM GENE, on one or more VGAM1685 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56887] It is yet further appreciated that a function of VGAM1685 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1685 include diagnosis, prevention and treatment of viral infection by Vesicular Stomatitis Indiana Virus. Specific functions, and accordingly utilities, of VGAM1685 correlate with, and may be deduced from, the identity of the host target genes which VGAM1685 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56888] Nucleotide sequences of the VGAM1685 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1685 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1685 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1685 are further described hereinbelow with reference to Table 1.

[56889] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1685 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1685 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56890] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1685 gene, herein designated VGAM is

inhibition of expression of VGAM1685 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1685 correlate with, and may be deduced from, the identity of the target genes which VGAM1685 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56891] TU3A (Accession NM\_007177) is a VGAM1685 host target gene. TU3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TU3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TU3A BINDING SITE, designated SEQ ID:14035, to the nucleotide sequence of VGAM1685 RNA, herein designated VGAM RNA, also designated SEQ ID:4396.

[56892] A function of VGAM1685 is therefore inhibition of TU3A (Accession NM\_007177). Accordingly, utilities of VGAM1685 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TU3A. LOC257481 (Accession XM\_028192) is another VGAM1685 host target gene. LOC257481 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257481, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257481 BINDING SITE, designated SEQ ID:30631, to the nucleotide sequence of VGAM1685 RNA, herein designated VGAM RNA, also designated SEQ ID:4396.

[56893] Another function of VGAM1685 is therefore inhibition of LOC257481 (Accession XM\_028192). Accordingly, utilities of VGAM1685 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257481. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1686 (VGAM1686) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56894] VGAM1686 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1686 was detected is described hereinabove with reference to Figs. 1-8.

[56895] VGAM1686 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vesicular Stomatitis In-

diana Virus. VGAM1686 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56896] VGAM1686 gene encodes a VGAM1686 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1686 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1686 precursor RNA is designated SEQ ID:1672, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1672 is located at position 2116 relative to the genome of Vesicular Stomatitis Indiana Virus.

[56897] VGAM1686 precursor RNA folds onto itself, forming VGAM1686 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56898] An enzyme complex designated DICER COMPLEX, `dices`



the VGAM1686 folded precursor RNA into VGAM1686 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1686 RNA is designated SEQ ID:4397, and is provided hereinbelow with reference to the sequence listing part.

[56899] VGAM1686 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1686 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1686 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56900] VGAM1686 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1686 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1686 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1686 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1686 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56901] The complementary binding of VGAM1686 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1686 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1686 host target RNA into VGAM1686 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56902] It is appreciated that VGAM1686 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1686 host target genes. The mRNA of each one of this plurality of VGAM1686 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1686 RNA, herein designated VGAM RNA, and which when bound by VGAM1686 RNA causes inhibition of translation of respective one or more VGAM1686 host target proteins.

[56903] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1686 gene, herein designated VGAM GENE, on one or more VGAM1686 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56904] It is yet further appreciated that a function of VGAM1686 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of viral infection by Vesicular Stomatitis Indiana Virus. Specific functions, and accordingly utilities, of VGAM1686 correlate with, and may be deduced from, the identity of the host target genes which VGAM1686 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56905] Nucleotide sequences of the VGAM1686 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1686 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1686 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1686 are further described hereinbelow with reference to Table 1.

[56906] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1686 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1686 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56907] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1686 gene, herein designated VGAM is inhibition of expression of VGAM1686 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1686 correlate with, and may be deduced from, the identity of the target genes which VGAM1686 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56908] ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 12 (ABCC12, Accession NM\_033226) is a VGAM1686 host target gene. ABCC12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCC12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC12 BINDING SITE,

designated SEQ ID:27072, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56909] A function of VGAM1686 is therefore inhibition of ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 12 (ABCC12, Accession NM\_033226), a gene which acts as a multispecific organic anion pump which can transport nucleotide analogs (by similarity). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC12. The function of ABCC12 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1246. Axin 1 (AXIN1, Accession XM\_027520) is another VGAM1686 host target gene. AXIN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AXIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AXIN1 BINDING SITE, designated SEQ ID:30518, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ

ID:4397.

[56910] Another function of VGAM1686 is therefore inhibition of Axin 1 (AXIN1, Accession XM\_027520). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AXIN1. Potassium Channel, Subfamily K, Member 5 (KCNK5, Accession NM\_003740) is another VGAM1686 host target gene. KCNK5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNK5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNK5 BINDING SITE, designated SEQ ID:9828, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56911] Another function of VGAM1686 is therefore inhibition of Potassium Channel, Subfamily K, Member 5 (KCNK5, Accession NM\_003740). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNK5. L1 Cell Adhesion Molecule (hydrocephalus, stenosis of aqueduct of Sylvius 1, MASA (mental retardation, aphasia, shuffling

gait and adducted thumbs) Syndrome, Spastic Paraplegia 1) (L1CAM, Accession NM\_000425) is another VGAM1686 host target gene. L1CAM BINDING SITE1 and L1CAM BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by L1CAM, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of L1CAM BINDING SITE1 and L1CAM BINDING SITE2, designated SEQ ID:6003 and SEQ ID:23431 respectively, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56912] Another function of VGAM1686 is therefore inhibition of L1 Cell Adhesion Molecule (hydrocephalus, stenosis of aqueduct of Sylvius 1, MASA (mental retardation, aphasia, shuffling gait and adducted thumbs) Syndrome, Spastic Paraplegia 1) (L1CAM, Accession NM\_000425). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with L1CAM. Peroxisome Biogenesis Factor 10 (PEX10, Accession NM\_002617) is another VGAM1686 host target gene. PEX10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA



encoded by PEX10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEX10 BINDING SITE, designated SEQ ID:8479, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56913] Another function of VGAM1686 is therefore inhibition of Peroxisome Biogenesis Factor 10 (PEX10, Accession NM\_002617). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEX10. Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 1 (p85 alpha) (PIK3R1, Accession XM\_043865) is another VGAM1686 host target gene. PIK3R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3R1 BINDING SITE, designated SEQ ID:34036, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56914] Another function of VGAM1686 is therefore inhibition of Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 1 (p85 alpha) (PIK3R1, Accession XM\_043865), a gene which acts as an adapter, for the insulin-stimulated increase in glucose uptake and glycogen synthesis. Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3R1. The function of PIK3R1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM826. Serine Hydroxymethyltransferase 1 (soluble) (SHMT1, Accession NM\_004169) is another VGAM1686 host target gene. SHMT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SHMT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHMT1 BINDING SITE, designated SEQ ID:10374, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56915] Another function of VGAM1686 is therefore inhibition of

Serine Hydroxymethyltransferase 1 (soluble) (SHMT1, Accession NM\_004169), a gene which interconverts serine and glycine. Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHMT1. The function of SHMT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM475. Tumor Necrosis Factor, Alpha-induced Protein 1 (endothelial) (TNFAIP1, Accession NM\_021137) is another VGAM1686 host target gene. TNFAIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFAIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFAIP1 BINDING SITE, designated SEQ ID:22113, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56916] Another function of VGAM1686 is therefore inhibition of Tumor Necrosis Factor, Alpha-induced Protein 1 (endothelial) (TNFAIP1, Accession NM\_021137). Accordingly, utilities of VGAM1686 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with TNFAIP1. Vang-like 2 (van gogh, *Drosophila*) (VANGL2, Accession XM\_049695) is another VGAM1686 host target gene. VANGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VANGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VANGL2 BINDING SITE, designated SEQ ID:35480, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56917] Another function of VGAM1686 is therefore inhibition of Vang-like 2 (van gogh, *Drosophila*) (VANGL2, Accession XM\_049695), a gene which may take part in defining the lateral boundary of floorplate differentiation. Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VANGL2. The function of VANGL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM111.DKFZP434J046 (Accession XM\_048258) is another VGAM1686 host target gene. DK-

FZP434J046 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP434J046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434J046 BINDING SITE, designated SEQ ID:35150, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56918] Another function of VGAM1686 is therefore inhibition of DKFZP434J046 (Accession XM\_048258). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434J046. FLJ10385 (Accession NM\_018081) is another VGAM1686 host target gene. FLJ10385 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10385, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10385 BINDING SITE, designated SEQ ID:19840, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56919] Another function of VGAM1686 is therefore inhibition of FLJ10385 (Accession NM\_018081). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10385. FLJ12876 (Accession NM\_022754) is another VGAM1686 host target gene. FLJ12876 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12876 BINDING SITE, designated SEQ ID:22987, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56920] Another function of VGAM1686 is therefore inhibition of FLJ12876 (Accession NM\_022754). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12876. FLJ20375 (Accession NM\_017794) is another VGAM1686 host target gene. FLJ20375 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20375, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20375 BINDING SITE, designated SEQ ID:19433, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56921] Another function of VGAM1686 is therefore inhibition of FLJ20375 (Accession NM\_017794). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20375. FLJ22625 (Accession NM\_024715) is another VGAM1686 host target gene. FLJ22625 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22625, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22625 BINDING SITE, designated SEQ ID:24042, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56922] Another function of VGAM1686 is therefore inhibition of FLJ22625 (Accession NM\_024715). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ22625. GR6 (Accession NM\_007354) is another VGAM1686 host target gene. GR6 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GR6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GR6 BINDING SITE, designated SEQ ID:14280, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56923] Another function of VGAM1686 is therefore inhibition of GR6 (Accession NM\_007354). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GR6. KIAA0451 (Accession NM\_014826) is another VGAM1686 host target gene. KIAA0451 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0451 BINDING SITE, designated SEQ ID:16807, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also des-



ignated SEQ ID:4397.

[56924] Another function of VGAM1686 is therefore inhibition of KIAA0451 (Accession NM\_014826). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0451. KIAA0544 (Accession XM\_048119) is another VGAM1686 host target gene. KIAA0544 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0544, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0544 BINDING SITE, designated SEQ ID:35109, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56925] Another function of VGAM1686 is therefore inhibition of KIAA0544 (Accession XM\_048119). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0544. MGC12435 (Accession NM\_031427) is another VGAM1686 host target gene. MGC12435 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC12435, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12435 BINDING SITE, designated SEQ ID:25423, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56926] Another function of VGAM1686 is therefore inhibition of MGC12435 (Accession NM\_031427). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12435. MGC29643 (Accession NM\_144586) is another VGAM1686 host target gene. MGC29643 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC29643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC29643 BINDING SITE, designated SEQ ID:29406, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56927] Another function of VGAM1686 is therefore inhibition of MGC29643 (Accession NM\_144586). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC29643. Oxysterol Binding Protein-like 5 (OSBPL5, Accession XM\_052567) is another VGAM1686 host target gene. OSBPL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL5 BINDING SITE, designated SEQ ID:35988, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56928] Another function of VGAM1686 is therefore inhibition of Oxysterol Binding Protein-like 5 (OSBPL5, Accession XM\_052567). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL5. Tubby Homolog (mouse) (TUB, Accession NM\_003320) is another VGAM1686 host target gene. TUB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of TUB BINDING SITE, designated SEQ ID:9319, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56929] Another function of VGAM1686 is therefore inhibition of Tubby Homolog (mouse) (TUB, Accession NM\_003320). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUB. LOC119188 (Accession XM\_058373) is another VGAM1686 host target gene. LOC119188 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC119188, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC119188 BINDING SITE, designated SEQ ID:36613, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56930] Another function of VGAM1686 is therefore inhibition of LOC119188 (Accession XM\_058373). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC119188. LOC145717 (Accession XM\_039771) is another VGAM1686 host target gene. LOC145717 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145717, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145717 BINDING SITE, designated SEQ ID:33190, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56931] Another function of VGAM1686 is therefore inhibition of LOC145717 (Accession XM\_039771). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145717. LOC146795 (Accession XM\_085593) is another VGAM1686 host target gene. LOC146795 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146795 BINDING SITE, designated SEQ ID:38244, to the nucleotide sequence of VGAM1686 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4397.

[56932] Another function of VGAM1686 is therefore inhibition of LOC146795 (Accession XM\_085593). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146795. LOC151176 (Accession XM\_098016) is another VGAM1686 host target gene. LOC151176 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151176, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151176 BINDING SITE, designated SEQ ID:41317, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56933] Another function of VGAM1686 is therefore inhibition of LOC151176 (Accession XM\_098016). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151176. LOC152453 (Accession XM\_087475) is another VGAM1686 host target gene. LOC152453 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152453, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152453 BINDING SITE, designated SEQ ID:39276, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56934] Another function of VGAM1686 is therefore inhibition of LOC152453 (Accession XM\_087475). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152453. LOC155061 (Accession XM\_088139) is another VGAM1686 host target gene. LOC155061 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC155061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155061 BINDING SITE, designated SEQ ID:39536, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56935] Another function of VGAM1686 is therefore inhibition of LOC155061 (Accession XM\_088139). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC155061. LOC197342 (Accession XM\_113869) is another VGAM1686 host target gene. LOC197342 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC197342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197342 BINDING SITE, designated SEQ ID:42488, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56936] Another function of VGAM1686 is therefore inhibition of LOC197342 (Accession XM\_113869). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197342. LOC201689 (Accession XM\_040608) is another VGAM1686 host target gene. LOC201689 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC201689, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201689 BINDING SITE, designated SEQ ID:33332, to



the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56937] Another function of VGAM1686 is therefore inhibition of LOC201689 (Accession XM\_040608). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201689. LOC221140 (Accession XM\_167908) is another VGAM1686 host target gene. LOC221140 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221140 BINDING SITE, designated SEQ ID:44907, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56938] Another function of VGAM1686 is therefore inhibition of LOC221140 (Accession XM\_167908). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221140. LOC222166 (Accession XM\_168425) is another VGAM1686 host target gene. LOC222166 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC222166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222166 BINDING SITE, designated SEQ ID:45151, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56939] Another function of VGAM1686 is therefore inhibition of LOC222166 (Accession XM\_168425). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222166. LOC254431 (Accession XM\_173024) is another VGAM1686 host target gene. LOC254431 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254431, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254431 BINDING SITE, designated SEQ ID:46290, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56940] Another function of VGAM1686 is therefore inhibition of LOC254431 (Accession XM\_173024). Accordingly, utilities

of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254431. LOC91974 (Accession XM\_041974) is another VGAM1686 host target gene. LOC91974 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91974, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91974 BINDING SITE, designated SEQ ID:33653, to the nucleotide sequence of VGAM1686 RNA, herein designated VGAM RNA, also designated SEQ ID:4397.

[56941] Another function of VGAM1686 is therefore inhibition of LOC91974 (Accession XM\_041974). Accordingly, utilities of VGAM1686 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91974. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1687 (VGAM1687) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56942] VGAM1687 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1687 was detected is described hereinabove with reference to Figs. 1-8.

[56943] VGAM1687 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1687 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56944] VGAM1687 gene encodes a VGAM1687 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1687 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1687 precursor RNA is designated SEQ ID:1673, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1673 is located at position 126333 relative to the genome of Chimpanzee Cytomegalovirus.

[56945] VGAM1687 precursor RNA folds onto itself, forming VGAM1687 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56946] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1687 folded precursor RNA into VGAM1687 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1687 RNA is designated SEQ ID:4398, and is provided hereinbelow with reference to the sequence listing part.

[56947] VGAM1687 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1687 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1687 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[56948] VGAM1687 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1687 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1687 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1687 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1687 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56949] The complementary binding of VGAM1687 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1687 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1687 host target RNA into VGAM1687 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56950] It is appreciated that VGAM1687 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1687 host target genes. The mRNA of each one of this plurality of VGAM1687 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1687 RNA, herein designated VGAM RNA, and which when bound by VGAM1687 RNA causes inhibition of translation of respective one or more VGAM1687 host target proteins.

[56951] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1687 gene, herein designated VGAM GENE, on one or more VGAM1687 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56952] It is yet further appreciated that a function of VGAM1687 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1687 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1687 correlate with, and may be deduced from, the identity of the host target genes which VGAM1687 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56953] Nucleotide sequences of the VGAM1687 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1687 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1687 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1687 are further  
described hereinbelow with reference to Table 1.

[56954] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1687 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1687 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[56955] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1687 gene, herein designated VGAM is  
inhibition of expression of VGAM1687 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1687 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1687  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[56956] Cadherin, EGF LAG Seven-pass G-type Receptor 1  
(flamingo homolog, Drosophila) (CELSR1, Accession

NM\_014246) is a VGAM1687 host target gene. CELSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CELSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CELSR1 BINDING SITE, designated SEQ ID:15516, to the nucleotide sequence of VGAM1687 RNA, herein designated VGAM RNA, also designated SEQ ID:4398.

[56957] A function of VGAM1687 is therefore inhibition of Cadherin, EGF LAG Seven-pass G-type Receptor 1 (flamingo homolog, Drosophila) (CELSR1, Accession NM\_014246), a gene which is involved in contact-mediated communication. Accordingly, utilities of VGAM1687 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CELSR1. The function of CELSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM459. Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 6 (SLC7A6, Accession NM\_003983) is another VGAM1687 host target gene. SLC7A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by SLC7A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A6 BINDING SITE, designated SEQ ID:10125, to the nucleotide sequence of VGAM1687 RNA, herein designated VGAM RNA, also designated SEQ ID:4398.

[56958] Another function of VGAM1687 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 6 (SLC7A6, Accession NM\_003983), a gene which is involved in mediating amino acid transport. Accordingly, utilities of VGAM1687 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A6. The function of SLC7A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM87. LOC120826 (Accession XM\_062302) is another VGAM1687 host target gene. LOC120826 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC120826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC120826 BINDING SITE, designated SEQ ID:37223, to the nucleotide sequence of VGAM1687 RNA, herein designated VGAM RNA, also designated SEQ ID:4398.

[56959] Another function of VGAM1687 is therefore inhibition of LOC120826 (Accession XM\_062302). Accordingly, utilities of VGAM1687 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120826. LOC160717 (Accession XM\_090457) is another VGAM1687 host target gene. LOC160717 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC160717, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160717 BINDING SITE, designated SEQ ID:40007, to the nucleotide sequence of VGAM1687 RNA, herein designated VGAM RNA, also designated SEQ ID:4398.

[56960] Another function of VGAM1687 is therefore inhibition of LOC160717 (Accession XM\_090457). Accordingly, utilities of VGAM1687 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160717. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1688 (VGAM1688) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56961] VGAM1688 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1688 was detected is described hereinabove with reference to Figs. 1–8.

[56962] VGAM1688 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1688 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56963] VGAM1688 gene encodes a VGAM1688 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1688 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1688 precursor RNA is designated SEQ ID:1674, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1674 is located at position 123345 relative to the genome of Chimpanzee Cytomegalovirus.

[56964] VGAM1688 precursor RNA folds onto itself, forming VGAM1688 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[56965] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1688 folded precursor RNA into VGAM1688 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1688 RNA is designated SEQ ID:4399, and is provided hereinbelow with reference to the sequence listing part.

[56966] VGAM1688 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1688 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1688 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56967] VGAM1688 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1688 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1688 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1688 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1688 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[56968] The complementary binding of VGAM1688 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1688 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1688 host target RNA into VGAM1688 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56969] It is appreciated that VGAM1688 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1688 host target genes. The mRNA of each one of this plurality of VGAM1688 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1688 RNA, herein designated VGAM RNA, and which when bound by VGAM1688 RNA causes inhibition of translation of respective one or more



VGAM1688 host target proteins.

[56970] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1688 gene, herein designated VGAM GENE, on one or more VGAM1688 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56971] It is yet further appreciated that a function of VGAM1688 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1688 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cy-

tomegalovirus. Specific functions, and accordingly utilities, of VGAM1688 correlate with, and may be deduced from, the identity of the host target genes which VGAM1688 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56972] Nucleotide sequences of the VGAM1688 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1688 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1688 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1688 are further described hereinbelow with reference to Table 1.

[56973] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1688 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1688 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56974] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1688 gene, herein designated VGAM is inhibition of expression of VGAM1688 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1688 correlate with, and may be deduced from, the identity of the target genes which VGAM1688 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56975] Extra Spindle Poles Like 1 (*S. cerevisiae*) (ESPL1, Accession NM\_012291) is a VGAM1688 host target gene. ESPL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ESPL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESPL1 BINDING SITE, designated SEQ ID:14630, to the nucleotide sequence of VGAM1688 RNA, herein designated VGAM RNA, also designated SEQ ID:4399.

[56976] A function of VGAM1688 is therefore inhibition of Extra Spindle Poles Like 1 (*S. cerevisiae*) (ESPL1, Accession NM\_012291). Accordingly, utilities of VGAM1688 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESPL1. KIAA0515 (Accession XM\_033380) is another VGAM1688 host target gene. KIAA0515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0515, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0515 BINDING SITE, designated SEQ ID:31918, to the nucleotide sequence of VGAM1688 RNA, herein designated VGAM RNA, also designated SEQ ID:4399.

[56977] Another function of VGAM1688 is therefore inhibition of KIAA0515 (Accession XM\_033380). Accordingly, utilities of VGAM1688 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0515. LOC255937 (Accession XM\_171129) is another VGAM1688 host target gene. LOC255937 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255937 BINDING SITE, designated SEQ ID:45931, to the nucleotide sequence of VGAM1688 RNA, herein designated VGAM RNA, also designated SEQ ID:4399.

[56978] Another function of VGAM1688 is therefore inhibition of LOC255937 (Accession XM\_171129). Accordingly, utilities of VGAM1688 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC255937. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1689 (VGAM1689) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[56979] VGAM1689 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1689 was detected is described hereinabove with reference to Figs. 1–8.

[56980] VGAM1689 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1689 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[56981] VGAM1689 gene encodes a VGAM1689 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1689 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1689 precursor RNA is desig-

nated SEQ ID:1675, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1675 is located at position 127857 relative to the genome of Chimpanzee Cytomegalovirus.

- [56982] VGAM1689 precursor RNA folds onto itself, forming VGAM1689 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [56983] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1689 folded precursor RNA into VGAM1689 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1689 RNA is designated SEQ ID:4400, and is provided hereinbelow with reference to the sequence

listing part.

[56984] VGAM1689 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1689 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1689 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[56985] VGAM1689 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1689 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1689 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1689 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1689 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[56986] The complementary binding of VGAM1689 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1689 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1689 host target RNA into VGAM1689 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[56987] It is appreciated that VGAM1689 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1689 host target genes. The mRNA of each one of this plurality of VGAM1689 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1689 RNA, herein designated VGAM



RNA, and which when bound by VGAM1689 RNA causes inhibition of translation of respective one or more VGAM1689 host target proteins.

[56988] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1689 gene, herein designated VGAM GENE, on one or more VGAM1689 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[56989] It is yet further appreciated that a function of VGAM1689 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1689 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1689 correlate with, and may be deduced from, the identity of the host target genes which VGAM1689 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[56990] Nucleotide sequences of the VGAM1689 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1689 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1689 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1689 are further described hereinbelow with reference to Table 1.

[56991] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1689 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1689 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[56992] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1689 gene, herein designated VGAM is

inhibition of expression of VGAM1689 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1689 correlate with, and may be deduced from, the identity of the target genes which VGAM1689 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[56993] Diacylglycerol O-acyltransferase Homolog 1 (mouse) (DGAT1, Accession XM\_035370) is a VGAM1689 host target gene. DGAT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DGAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGAT1 BINDING SITE, designated SEQ ID:32236, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[56994] A function of VGAM1689 is therefore inhibition of Diacylglycerol O-acyltransferase Homolog 1 (mouse) (DGAT1, Accession XM\_035370). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGAT1. Protein Phosphatase 2, Regulatory Subunit B (B56), Alpha

Isoform (PPP2R5A, Accession NM\_006243) is another VGAM1689 host target gene. PPP2R5A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPP2R5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R5A BINDING SITE, designated SEQ ID:12910, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[56995] Another function of VGAM1689 is therefore inhibition of Protein Phosphatase 2, Regulatory Subunit B (B56), Alpha Isoform (PPP2R5A, Accession NM\_006243), a gene which is a regulatory subunit of protein phosphatase 2A. Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R5A. The function of PPP2R5A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675. Roundabout, Axon Guidance Receptor, Homolog 1 (Drosophila) (ROBO1, Accession NM\_133631) is another VGAM1689 host target gene. ROBO1 BINDING SITE is HOST TARGET

binding site found in the 5` untranslated region of mRNA encoded by ROBO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROBO1 BINDING SITE, designated SEQ ID:28584, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[56996] Another function of VGAM1689 is therefore inhibition of Roundabout, Axon Guidance Receptor, Homolog 1 (Drosophila) (ROBO1, Accession NM\_133631), a gene which is an axon guidance receptor. Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROBO1. The function of ROBO1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM37. Short Stature Homeobox (SHOX, Accession NM\_000451) is another VGAM1689 host target gene. SHOX BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SHOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of SHOX BINDING SITE, designated SEQ ID:6058, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[56997] Another function of VGAM1689 is therefore inhibition of Short Stature Homeobox (SHOX, Accession NM\_000451). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHOX. Telomeric Repeat Binding Factor 2 (TERF2, Accession NM\_005652) is another VGAM1689 host target gene. TERF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TERF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TERF2 BINDING SITE, designated SEQ ID:12188, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[56998] Another function of VGAM1689 is therefore inhibition of Telomeric Repeat Binding Factor 2 (TERF2, Accession NM\_005652), a gene which plays a key role in the protective activity of telomeres. Accordingly, utilities of

VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRF2. The function of TRF2 has been established by previous studies. Van Steensel et al. (1998) showed that the human telomeric protein TRF2 plays a key role in the protective activity of telomeres. A dominant-negative allele of TRF2 induced end-to-end chromosome fusions detectable in metaphase and anaphase cells. Telomeric DNA persisted at the fusions, demonstrating that TTAGGG repeats per se are not sufficient for telomere integrity. Molecular analysis suggested that the fusions represented ligation of telomeres that have lost their single-stranded G-tails. Van Steensel et al. (1998) concluded that TRF2 may protect chromosome ends by maintaining the correct structure at telomere termini. In addition, expression of mutant forms of TRF2 induced a growth arrest with characteristics of senescence. These results raise the possibility that chromosome end fusions and senescence in primary human cells may be caused by loss of TRF2 from shortened telomeres. Karlseder et al. (2002) reported that overexpression of TRF2 increased the rate of telomere shortening in primary cells without accelerating senescence. TRF2 reduced the senescence setpoint, defined as telomere

length at senescence, from 7 to 4 kb. TRF2 protected critically short telomeres from fusion and repressed chromosome-end fusions in presenescent cultures, which explained the ability of TRF2 to delay senescence. Thus, Karlseder et al. (2002) concluded that replicative senescence is induced by a change in the protected status of shortened telomeres rather than by a complete loss of telomeric DNA.

[56999] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57000] van Steensel, B.; Smogorzewska, A.; de Lange, T. : TRF2 protects human telomeres from end-to-end fusions. *Cell* 92: 401–413, 1998. ; and

[57001] Karlseder, J.; Smogorzewska, A.; de Lange, T. : Senescence induced by altered telomere state, not telomere loss. *Science* 295: 2446–2449, 2002.

[57002] Further studies establishing the function and utilities of TERF2 are found in John Hopkins OMIM database record ID 602027, and in cited publications numbered 9496–6665, 9622–9623, 6666–666 and 7146 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.X-ray Repair Comple–



menting Defective Repair In Chinese Hamster Cells 3 (XRCC3, Accession NM\_005432) is another VGAM1689 host target gene. XRCC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XRCC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XRCC3 BINDING SITE, designated SEQ ID:11909, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57003] Another function of VGAM1689 is therefore inhibition of X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 3 (XRCC3, Accession NM\_005432), a gene which is required for meiotic recombination, synaptonemal complex formation and cell cycle progression. Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XRCC3. The function of XRCC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1290. Chromosome 21 Open Reading Frame 4 (C21orf4, Accession NM\_006134)

is another VGAM1689 host target gene. C21orf4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C21orf4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf4 BINDING SITE, designated SEQ ID:12776, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57004] Another function of VGAM1689 is therefore inhibition of Chromosome 21 Open Reading Frame 4 (C21orf4, Accession NM\_006134). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf4. Di-Ras2 (Accession NM\_017594) is another VGAM1689 host target gene. Di-Ras2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Di-Ras2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Di-Ras2 BINDING SITE, designated SEQ ID:19043, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ

ID:4400.

[57005] Another function of VGAM1689 is therefore inhibition of Di-Ras2 (Accession NM\_017594). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Di-Ras2. DKFZp761G2113 (Accession XM\_046017) is another VGAM1689 host target gene. DKFZp761G2113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761G2113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761G2113 BINDING SITE, designated SEQ ID:34640, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57006] Another function of VGAM1689 is therefore inhibition of DKFZp761G2113 (Accession XM\_046017). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761G2113. FLJ14251 (Accession NM\_024881) is another VGAM1689 host target gene. FLJ14251 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by FLJ14251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14251 BINDING SITE, designated SEQ ID:24323, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57007] Another function of VGAM1689 is therefore inhibition of FLJ14251 (Accession NM\_024881). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14251. Microtubule-associated Protein 1 Light Chain 3 Alpha (MAP1LC3A, Accession NM\_032514) is another VGAM1689 host target gene. MAP1LC3A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAP1LC3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP1LC3A BINDING SITE, designated SEQ ID:26265, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57008] Another function of VGAM1689 is therefore inhibition of

Microtubule-associated Protein 1 Light Chain 3 Alpha (MAP1LC3A, Accession NM\_032514). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP1LC3A. RASD Family, Member 2 (RASD2, Accession NM\_014310) is another VGAM1689 host target gene. RASD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASD2 BINDING SITE, designated SEQ ID:15603, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57009] Another function of VGAM1689 is therefore inhibition of RASD Family, Member 2 (RASD2, Accession NM\_014310). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASD2. Sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase) (SIAT8C, Accession NM\_015879) is another VGAM1689 host target gene. SIAT8C BINDING SITE is HOST TARGET

binding site found in the 5' untranslated region of mRNA encoded by SIAT8C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT8C BINDING SITE, designated SEQ ID:18027, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57010] Another function of VGAM1689 is therefore inhibition of Sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase) (SIAT8C, Accession NM\_015879). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT8C. LOC124930 (Accession XM\_058867) is another VGAM1689 host target gene. LOC124930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124930 BINDING SITE, designated SEQ ID:36767, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4400.

[57011] Another function of VGAM1689 is therefore inhibition of LOC124930 (Accession XM\_058867). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124930. LOC127534 (Accession XM\_060532) is another VGAM1689 host target gene. LOC127534 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC127534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127534 BINDING SITE, designated SEQ ID:37170, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57012] Another function of VGAM1689 is therefore inhibition of LOC127534 (Accession XM\_060532). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127534. LOC129566 (Accession XM\_065294) is another VGAM1689 host target gene. LOC129566 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC129566, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129566 BINDING SITE, designated SEQ ID:37279, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57013] Another function of VGAM1689 is therefore inhibition of LOC129566 (Accession XM\_065294). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129566. LOC146957 (Accession XM\_085652) is another VGAM1689 host target gene. LOC146957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146957 BINDING SITE, designated SEQ ID:38281, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57014] Another function of VGAM1689 is therefore inhibition of LOC146957 (Accession XM\_085652). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC146957. LOC147136 (Accession XM\_085716) is another VGAM1689 host target gene. LOC147136 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC147136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147136 BINDING SITE, designated SEQ ID:38301, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57015] Another function of VGAM1689 is therefore inhibition of LOC147136 (Accession XM\_085716). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147136. LOC153480 (Accession XM\_053483) is another VGAM1689 host target gene. LOC153480 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC153480, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153480 BINDING SITE, designated SEQ ID:36089, to

the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57016] Another function of VGAM1689 is therefore inhibition of LOC153480 (Accession XM\_053483). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153480. LOC161635 (Accession XM\_172921) is another VGAM1689 host target gene. LOC161635 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC161635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161635 BINDING SITE, designated SEQ ID:46187, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57017] Another function of VGAM1689 is therefore inhibition of LOC161635 (Accession XM\_172921). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161635. LOC222865 (Accession XM\_167242) is another VGAM1689 host target gene. LOC222865 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC222865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222865 BINDING SITE, designated SEQ ID:44622, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57018] Another function of VGAM1689 is therefore inhibition of LOC222865 (Accession XM\_167242). Accordingly, utilities of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222865. LOC253962 (Accession XM\_172968) is another VGAM1689 host target gene. LOC253962 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253962 BINDING SITE, designated SEQ ID:46225, to the nucleotide sequence of VGAM1689 RNA, herein designated VGAM RNA, also designated SEQ ID:4400.

[57019] Another function of VGAM1689 is therefore inhibition of LOC253962 (Accession XM\_172968). Accordingly, utilities

of VGAM1689 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253962. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1690 (VGAM1690) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57020] VGAM1690 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1690 was detected is described hereinabove with reference to Figs. 1-8.

[57021] VGAM1690 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1690 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57022] VGAM1690 gene encodes a VGAM1690 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1690 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1690 precursor RNA is designated SEQ ID:1676, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1676 is located at position 49102 relative to the genome of Ectocarpus Siliculosus Virus.

- [57023] VGAM1690 precursor RNA folds onto itself, forming VGAM1690 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [57024] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1690 folded precursor RNA into VGAM1690 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1690 RNA is designated SEQ ID:4401, and

is provided hereinbelow with reference to the sequence listing part.

[57025] VGAM1690 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1690 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1690 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[57026] VGAM1690 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1690 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1690 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1690 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1690 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57027] The complementary binding of VGAM1690 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1690 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1690 host target RNA into VGAM1690 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57028] It is appreciated that VGAM1690 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1690 host target genes. The mRNA of each one of this plurality of VGAM1690 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1690 RNA, herein designated VGAM RNA, and which when bound by VGAM1690 RNA causes inhibition of translation of respective one or more VGAM1690 host target proteins.

[57029] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1690 gene, herein designated VGAM GENE, on one or more VGAM1690 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57030] It is yet further appreciated that a function of VGAM1690 is inhibition of expression of host target genes, as part of



a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1690 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1690 correlate with, and may be deduced from, the identity of the host target genes which VGAM1690 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57031] Nucleotide sequences of the VGAM1690 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1690 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1690 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1690 are further described hereinbelow with reference to Table 1.

[57032] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1690 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1690 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57033] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1690 gene, herein designated VGAM is inhibition of expression of VGAM1690 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1690 correlate with, and may be deduced from, the identity of the target genes which VGAM1690 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57034] Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11, Accession NM\_002474) is a VGAM1690 host target gene. MYH11 BINDING SITE1 and MYH11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MYH11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYH11 BINDING SITE1 and MYH11 BINDING SITE2, designated SEQ ID:8299 and SEQ ID:23141 respectively, to the nucleotide sequence of VGAM1690 RNA, herein designated VGAM RNA, also designated SEQ ID:4401.

[57035] A function of VGAM1690 is therefore inhibition of Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11, Accession NM\_002474), a gene which is involved in muscle contraction. Accordingly, utilities of VGAM1690 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with MYH11. The function of MYH11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. PANK (Accession NM\_138316) is another VGAM1690 host target gene. PANK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PANK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PANK BINDING SITE, designated SEQ ID:28713, to the nucleotide sequence of VGAM1690 RNA, herein designated VGAM RNA, also designated SEQ ID:4401.

[57036] Another function of VGAM1690 is therefore inhibition of PANK (Accession NM\_138316). Accordingly, utilities of VGAM1690 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PANK. LOC126755 (Accession XM\_059074) is another VGAM1690 host target gene. LOC126755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126755, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126755 BINDING SITE, designated SEQ ID:36859, to the nucleotide sequence of VGAM1690 RNA, herein designated VGAM RNA, also designated SEQ ID:4401.

[57037] Another function of VGAM1690 is therefore inhibition of LOC126755 (Accession XM\_059074). Accordingly, utilities of VGAM1690 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126755. LOC164382 (Accession XM\_104390) is another VGAM1690 host target gene. LOC164382 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164382 BINDING SITE, designated SEQ ID:42166, to the nucleotide sequence of VGAM1690 RNA, herein designated VGAM RNA, also designated SEQ ID:4401.

[57038] Another function of VGAM1690 is therefore inhibition of LOC164382 (Accession XM\_104390). Accordingly, utilities of VGAM1690 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC164382. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1691 (VGAM1691) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57039] VGAM1691 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1691 was detected is described hereinabove with reference to Figs. 1–8.

[57040] VGAM1691 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1691 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57041] VGAM1691 gene encodes a VGAM1691 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1691 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1691 precursor RNA is designated SEQ ID:1677, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1677 is located at position 46991 relative to the genome of Ectocarpus Siliculosus Virus.

- [57042] VGAM1691 precursor RNA folds onto itself, forming VGAM1691 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [57043] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1691 folded precursor RNA into VGAM1691 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1691 RNA is designated SEQ ID:4402, and is provided hereinbelow with reference to the sequence listing part.

[57044] VGAM1691 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1691 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1691 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57045] VGAM1691 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1691 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1691 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1691 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1691 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[57046] The complementary binding of VGAM1691 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1691 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1691 host target RNA into VGAM1691 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57047] It is appreciated that VGAM1691 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1691 host target genes. The mRNA of each one of this plurality of VGAM1691 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1691 RNA, herein designated VGAM RNA, and which when bound by VGAM1691 RNA causes



inhibition of translation of respective one or more VGAM1691 host target proteins.

[57048] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1691 gene, herein designated VGAM GENE, on one or more VGAM1691 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57049] It is yet further appreciated that a function of VGAM1691 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1691 include diagnosis, prevention and

treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1691 correlate with, and may be deduced from, the identity of the host target genes which VGAM1691 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57050] Nucleotide sequences of the VGAM1691 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1691 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1691 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1691 are further described hereinbelow with reference to Table 1.

[57051] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1691 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1691 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57052] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1691 gene, herein designated VGAM is inhibition of expression of VGAM1691 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1691 correlate with, and may be deduced from, the identity of the target genes which VGAM1691 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57053] ABH (Accession XM\_007409) is a VGAM1691 host target gene. ABH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABH BINDING SITE, designated SEQ ID:30053, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57054] A function of VGAM1691 is therefore inhibition of ABH (Accession XM\_007409). Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABH. CD244 (Accession NM\_016382) is another VGAM1691 host target gene. CD244 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD244, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD244 BINDING SITE, designated SEQ ID:18523, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57055] Another function of VGAM1691 is therefore inhibition of CD244 (Accession NM\_016382), a gene which can interfere with a step as proximal as phosphorylation of an activation receptor. Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD244. The function of CD244 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. Cleavage and Polyadenylation Specific Factor 4, 30kDa (CPSF4, Accession NM\_006693) is another VGAM1691 host target gene. CPSF4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPSF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPSF4 BINDING SITE, designated SEQ ID:13513, to the nucleotide sequence of

VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57056] Another function of VGAM1691 is therefore inhibition of Cleavage and Polyadenylation Specific Factor 4, 30kDa (CPSF4, Accession NM\_006693), a gene which may bind DNA. Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPSF4. The function of CPSF4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM998. IL2-inducible T-cell Kinase (ITK, Accession NM\_005546) is another VGAM1691 host target gene. ITK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITK BINDING SITE, designated SEQ ID:12074, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57057] Another function of VGAM1691 is therefore inhibition of IL2-inducible T-cell Kinase (ITK, Accession NM\_005546), a

gene which plays a role in t cell proliferation and differentiation. Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITK. The function of ITK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM288. Calsyntenin 2 (CLSTN2, Accession NM\_022131) is another VGAM1691 host target gene. CLSTN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLSTN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLSTN2 BINDING SITE, designated SEQ ID:22692, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57058] Another function of VGAM1691 is therefore inhibition of Calsyntenin 2 (CLSTN2, Accession NM\_022131). Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLSTN2. CMG2 (Accession NM\_058172) is another VGAM1691 host target gene. CMG2 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CMG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CMG2 BINDING SITE, designated SEQ ID:27717, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57059] Another function of VGAM1691 is therefore inhibition of CMG2 (Accession NM\_058172). Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CMG2. FLJ23186 (Accession XM\_017088) is another VGAM1691 host target gene. FLJ23186 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23186, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23186 BINDING SITE, designated SEQ ID:30296, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57060] Another function of VGAM1691 is therefore inhibition of

FLJ23186 (Accession XM\_017088). Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23186. KIAA0367 (Accession XM\_041018) is another VGAM1691 host target gene. KIAA0367 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0367, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0367 BINDING SITE, designated SEQ ID:33416, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57061] Another function of VGAM1691 is therefore inhibition of KIAA0367 (Accession XM\_041018). Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0367. Solute Carrier Family 21 (organic anion transporter), Member 14 (SLC21A14, Accession NM\_017435) is another VGAM1691 host target gene. SLC21A14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC21A14, corresponding to a HOST TARGET binding site such as BINDING



SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC21A14 BINDING SITE, designated SEQ ID:18890, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57062] Another function of VGAM1691 is therefore inhibition of Solute Carrier Family 21 (organic anion transporter), Member 14 (SLC21A14, Accession NM\_017435). Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC21A14. LOC116411 (Accession XM\_058095) is another VGAM1691 host target gene. LOC116411 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC116411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116411 BINDING SITE, designated SEQ ID:36573, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57063] Another function of VGAM1691 is therefore inhibition of LOC116411 (Accession XM\_058095). Accordingly, utilities

of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116411. LOC157349 (Accession XM\_088298) is another VGAM1691 host target gene. LOC157349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157349 BINDING SITE, designated SEQ ID:39587, to the nucleotide sequence of VGAM1691 RNA, herein designated VGAM RNA, also designated SEQ ID:4402.

[57064] Another function of VGAM1691 is therefore inhibition of LOC157349 (Accession XM\_088298). Accordingly, utilities of VGAM1691 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157349. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1692 (VGAM1692) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57065] VGAM1692 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1692 was detected is described hereinabove with reference to Figs. 1–8.

[57066] VGAM1692 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1692 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57067] VGAM1692 gene encodes a VGAM1692 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1692 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1692 precursor RNA is designated SEQ ID:1678, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1678 is located at position 52063 relative to the genome of Ectocarpus Siliculosus Virus.

[57068] VGAM1692 precursor RNA folds onto itself, forming VGAM1692 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57069] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1692 folded precursor RNA into VGAM1692 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1692 RNA is designated SEQ ID:4403, and is provided hereinbelow with reference to the sequence listing part.

[57070] VGAM1692 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1692 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1692 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[57071] VGAM1692 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1692 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1692 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1692 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1692 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57072] The complementary binding of VGAM1692 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1692 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1692 host target RNA into VGAM1692 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57073] It is appreciated that VGAM1692 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1692 host target genes. The mRNA of each one of this plurality of VGAM1692 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1692 RNA, herein designated VGAM RNA, and which when bound by VGAM1692 RNA causes inhibition of translation of respective one or more VGAM1692 host target proteins.

[57074] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1692 gene, herein designated VGAM GENE, on one or more VGAM1692 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57075] It is yet further appreciated that a function of VGAM1692 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1692 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1692 correlate with, and may be deduced from, the identity of the host target genes which VGAM1692 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57076] Nucleotide sequences of the VGAM1692 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1692 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1692 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1692 are further  
described hereinbelow with reference to Table 1.

[57077] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1692 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1692 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[57078] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1692 gene, herein designated VGAM is  
inhibition of expression of VGAM1692 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1692 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1692  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[57079] Protein Kinase C, Nu (PRKCN, Accession NM\_005813) is a  
VGAM1692 host target gene. PRKCN BINDING SITE is HOST



TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKCN BINDING SITE, designated SEQ ID:12400, to the nucleotide sequence of VGAM1692 RNA, herein designated VGAM RNA, also designated SEQ ID:4403.

[57080] A function of VGAM1692 is therefore inhibition of Protein Kinase C,  $\alpha$  (PRKCN, Accession NM\_005813). Accordingly, utilities of VGAM1692 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKCN. WAS Protein Family, Member 3 (WASF3, Accession NM\_006646) is another VGAM1692 host target gene. WASF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WASF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WASF3 BINDING SITE, designated SEQ ID:13443, to the nucleotide sequence of VGAM1692 RNA, herein designated VGAM RNA, also designated SEQ ID:4403.

[57081] Another function of VGAM1692 is therefore inhibition of WAS Protein Family, Member 3 (WASF3, Accession NM\_006646), a gene which stimulates actin polymerization. Accordingly, utilities of VGAM1692 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WASF3. The function of WASF3 has been established by previous studies. The actin cytoskeleton plays critical roles in cell morphologic changes and

motility. Rho family small GTPases such as Rho (see OMIM Ref. No. 165370), RAC (see OMIM Ref. No. 602048), and CDC42 (OMIM Ref. No. 116952) organize the actin cytoskeleton. Other major players in actin-based motility are the 7 members of the ARP2/3 complex (see OMIM Ref. No. 604221). The Wiskott–Aldrich syndrome protein (WASP; 301000) and WASP-like (WASL; 605056) are among the downstream effector molecules involved in the transmission of signals from tyrosine kinase receptors and small GTPases to the actin cytoskeleton. WASF1 (OMIM Ref. No. 605035) is also involved in actin reorganization, but its expression is restricted to brain. By searching an EST database for homologs of WASF1 and by screening cDNA libraries, Suetsugu et al. (1999) identified WASF2 (OMIM Ref. No. 605068) and WASF3, which they termed WAVE2 and WAVE3, respectively. The predicted 502-amino acid WASF3 protein shares 48% amino acid identity with WASF1. Northern blot analysis revealed that, like WASF1, WASF3 expression is strongest in brain, although weak expression was detected in kidney and liver. SDS-PAGE analysis showed that, like other WASP family members, WASF3 binds actin through its C-terminal verprolin homology (VPH) domain. Immunofluorescence mi-

croscopy demonstrated that ectopically expressed WASF3 induces abnormal actin clusters. These actin cluster formations were suppressed by deletion of the VPH domain of WASF3.

[57082] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57083] Nagase, T.; Ishikawa, K.; Suyama, M.; Kikuno, R.; Hiro-sawa, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. XII. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro. DNA Res. 5: 355–364, 1998. ; and

[57084] Suetsugu, S.; Miki, H.; Takenawa, T. : Identification of two human WAVE/SCAR homologues as general actin regulatory molecules which associate with the Arp2/3 complex. Biochem. Biophys.

[57085] Further studies establishing the function and utilities of WASF3 are found in John Hopkins OMIM database record ID 605068, and in cited publications numbered 493 and 6593 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Calcium/calmodulin-dependent Protein Kinase Ki-

nase 1, Alpha (CAMKK1, Accession NM\_032294) is another VGAM1692 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26063, to the nucleotide sequence of VGAM1692 RNA, herein designated VGAM RNA, also designated SEQ ID:4403.

[57086] Another function of VGAM1692 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294). Accordingly, utilities of VGAM1692 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1693 (VGAM1693) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57087] VGAM1693 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1693 was detected is described hereinabove with reference to Figs. 1–8.

[57088] VGAM1693 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1693 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57089] VGAM1693 gene encodes a VGAM1693 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1693 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1693 precursor RNA is designated SEQ ID:1679, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1679 is located at position 54673 relative to the genome of Ectocarpus Siliculosus Virus.

[57090] VGAM1693 precursor RNA folds onto itself, forming VGAM1693 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57091] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1693 folded precursor RNA into VGAM1693 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1693 RNA is designated SEQ ID:4404, and is provided hereinbelow with reference to the sequence listing part.

[57092] VGAM1693 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1693 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1693 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57093] VGAM1693 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1693 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1693 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1693 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1693 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57094] The complementary binding of VGAM1693 RNA, herein



designated VGAM RNA, to host target binding sites on VGAM1693 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1693 host target RNA into VGAM1693 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57095] It is appreciated that VGAM1693 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1693 host target genes. The mRNA of each one of this plurality of VGAM1693 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1693 RNA, herein designated VGAM RNA, and which when bound by VGAM1693 RNA causes inhibition of translation of respective one or more VGAM1693 host target proteins.

[57096] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1693 gene, herein designated VGAM GENE, on one or more VGAM1693 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57097] It is yet further appreciated that a function of VGAM1693 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1693 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1693 correlate with, and may be deduced from, the identity of the host target genes which VGAM1693 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57098] Nucleotide sequences of the VGAM1693 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1693 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1693 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1693 are further described hereinbelow with reference to Table 1.

[57099] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1693 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1693 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57100] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1693 gene, herein designated VGAM is inhibition of expression of VGAM1693 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1693 correlate with, and may be deduced from, the identity of the target genes which VGAM1693 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57101] Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM\_096169) is a VGAM1693 host target gene. INPP5D BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by INPP5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5D BINDING SITE, designated SEQ ID:40302, to the nucleotide sequence of VGAM1693 RNA, herein designated VGAM RNA, also designated SEQ ID:4404.

[57102] A function of VGAM1693 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM\_096169), a gene which hydrolyzes Ins(1,3,4,5)P<sub>4</sub> and PtdIns(3,4,5)P<sub>3</sub>; contains an SH2-domain. Accordingly, utilities of VGAM1693 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5D. The function of INPP5D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM64. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1694 (VGAM1694) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host

target genes is known in the art.

[57103] VGAM1694 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1694 was detected is described hereinabove with reference to Figs. 1–8.

[57104] VGAM1694 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1694 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57105] VGAM1694 gene encodes a VGAM1694 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1694 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1694 precursor RNA is designated SEQ ID:1680, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1680 is located at position 50970 relative to the genome of Ectocarpus Siliculosus Virus.

[57106] VGAM1694 precursor RNA folds onto itself, forming VGAM1694 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57107] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1694 folded precursor RNA into VGAM1694 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1694 RNA is designated SEQ ID:4405, and is provided hereinbelow with reference to the sequence listing part.

[57108] VGAM1694 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1694 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1694 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[57109] VGAM1694 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1694 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1694 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1694 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1694 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[57110] The complementary binding of VGAM1694 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1694 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1694 host target RNA into VGAM1694 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57111] It is appreciated that VGAM1694 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1694 host target genes. The mRNA of each one of this plurality of VGAM1694 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1694 RNA, herein designated VGAM RNA, and which when bound by VGAM1694 RNA causes inhibition of translation of respective one or more VGAM1694 host target proteins.

[57112] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1694 gene, herein designated VGAM GENE, on one



or more VGAM1694 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57113] It is yet further appreciated that a function of VGAM1694 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1694 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1694 correlate with, and may be deduced from, the identity of the host target genes which VGAM1694 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57114] Nucleotide sequences of the VGAM1694 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1694 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1694 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1694 are further described hereinbelow with reference to Table 1.

[57115] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1694 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1694 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57116] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1694 gene, herein designated VGAM is inhibition of expression of VGAM1694 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1694 correlate with, and may be deduced from, the identity of the target genes which VGAM1694 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57117] Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D,

Accession XM\_096169) is a VGAM1694 host target gene. INPP5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INPP5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5D BINDING SITE, designated SEQ ID:40302, to the nucleotide sequence of VGAM1694 RNA, herein designated VGAM RNA, also designated SEQ ID:4405.

[57118] A function of VGAM1694 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM\_096169), a gene which hydrolyzes Ins(1,3,4,5)P<sub>4</sub> and PtdIns(3,4,5)P<sub>3</sub>; contains an SH2-domain. Accordingly, utilities of VGAM1694 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5D. The function of INPP5D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM64. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1695 (VGAM1695)

viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57119] VGAM1695 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1695 was detected is described hereinabove with reference to Figs. 1–8.

[57120] VGAM1695 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1695 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57121] VGAM1695 gene encodes a VGAM1695 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1695 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1695 precursor RNA is designated SEQ ID:1681, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1681 is located at position 51375 relative to the genome of Ectocarpus Siliculosus Virus.

[57122] VGAM1695 precursor RNA folds onto itself, forming

VGAM1695 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57123] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1695 folded precursor RNA into VGAM1695 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1695 RNA is designated SEQ ID:4406, and is provided hereinbelow with reference to the sequence listing part.

[57124] VGAM1695 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1695 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1695 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57125] VGAM1695 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1695 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1695 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1695 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1695 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57126] The complementary binding of VGAM1695 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1695 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1695 host target RNA into VGAM1695 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57127] It is appreciated that VGAM1695 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1695 host target genes. The mRNA of each one of this plurality of VGAM1695 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1695 RNA, herein designated VGAM RNA, and which when bound by VGAM1695 RNA causes inhibition of translation of respective one or more VGAM1695 host target proteins.

[57128] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1695 gene, herein designated VGAM GENE, on one or more VGAM1695 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57129] It is yet further appreciated that a function of VGAM1695 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1695 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1695 correlate with, and may be deduced from, the identity of the host target genes which VGAM1695 binds



and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57130] Nucleotide sequences of the VGAM1695 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1695 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1695 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1695 are further described hereinbelow with reference to Table 1.

[57131] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1695 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1695 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57132] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1695 gene, herein designated VGAM is inhibition of expression of VGAM1695 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1695 correlate with, and may be deduced from, the identity of the target genes which VGAM1695 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[57133] Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM\_096169) is a VGAM1695 host target gene. INPP5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INPP5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5D BINDING SITE, designated SEQ ID:40302, to the nucleotide sequence of VGAM1695 RNA, herein designated VGAM RNA, also designated SEQ ID:4406.

[57134] A function of VGAM1695 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM\_096169), a gene which hydrolyzes Ins(1,3,4,5)P<sub>4</sub> and PtdIns(3,4,5)P<sub>3</sub>; contains an SH2-domain. Accordingly, utilities of VGAM1695 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5D. The function of INPP5D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM64. Fig. 1 further provides a conceptual description of a novel bioinformatically de-

tected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1696 (VGAM1696) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57135] VGAM1696 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1696 was detected is described hereinabove with reference to Figs. 1–8.

[57136] VGAM1696 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1696 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57137] VGAM1696 gene encodes a VGAM1696 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1696 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1696 precursor RNA is designated SEQ ID:1682, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1682 is located at position 52738 relative to the

genome of Ectocarpus Siliculosus Virus.

[57138] VGAM1696 precursor RNA folds onto itself, forming VGAM1696 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57139] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1696 folded precursor RNA into VGAM1696 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1696 RNA is designated SEQ ID:4407, and is provided hereinbelow with reference to the sequence listing part.

[57140] VGAM1696 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1696 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1696 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57141] VGAM1696 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1696 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1696 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1696 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1696 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57142] The complementary binding of VGAM1696 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1696 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1696 host target RNA into VGAM1696 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57143] It is appreciated that VGAM1696 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1696 host target genes. The mRNA of each one of this plurality of VGAM1696 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1696 RNA, herein designated VGAM RNA, and which when bound by VGAM1696 RNA causes inhibition of translation of respective one or more VGAM1696 host target proteins.

[57144] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1696 gene, herein designated VGAM GENE, on one or more VGAM1696 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57145] It is yet further appreciated that a function of VGAM1696 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of

VGAM1696 correlate with, and may be deduced from, the identity of the host target genes which VGAM1696 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57146] Nucleotide sequences of the VGAM1696 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1696 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1696 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1696 are further described hereinbelow with reference to Table 1.

[57147] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1696 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1696 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57148] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1696 gene, herein designated VGAM is inhibition of expression of VGAM1696 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1696 correlate with, and may be deduced



from, the identity of the target genes which VGAM1696 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57149] 5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868) is a VGAM1696 host target gene. HTR2C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HTR2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR2C BINDING SITE, designated SEQ ID:6534, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57150] A function of VGAM1696 is therefore inhibition of 5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868), a gene which activates phospholipase C and regulates intracellular calcium flux. Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR2C. The function of HTR2C and its association with various diseases and clinical conditions, has been established by previous studies, as described here-

inabove with reference to VGAM1052.Inositol

1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224) is another VGAM1696 host target gene.

ITPR3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ITPR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR3 BINDING SITE, designated SEQ ID:7998, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57151] Another function of VGAM1696 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224), a gene which may be responsible for calcium release from intracellular stores. Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR3. The function of ITPR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM310.Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294) is another VGAM1696 host target gene.

CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26067, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57152] Another function of VGAM1696 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294). Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. FLJ21432 (Accession NM\_024551) is another VGAM1696 host target gene. FLJ21432 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21432 BINDING SITE, designated SEQ ID:23769, to the nucleotide sequence of VGAM1696 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4407.

[57153] Another function of VGAM1696 is therefore inhibition of FLJ21432 (Accession NM\_024551). Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21432. LGP1 (Accession NM\_032484) is another VGAM1696 host target gene. LGP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LGP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGP1 BINDING SITE, designated SEQ ID:26231, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57154] Another function of VGAM1696 is therefore inhibition of LGP1 (Accession NM\_032484). Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGP1. Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010) is another VGAM1696 host target gene. MAP2K4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

MAP2K4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K4 BINDING SITE, designated SEQ ID:8918, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57155] Another function of VGAM1696 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010). Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K4. MGC14161 (Accession NM\_032892) is another VGAM1696 host target gene. MGC14161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC14161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14161 BINDING SITE, designated SEQ ID:26718, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57156] Another function of VGAM1696 is therefore inhibition of

MGC14161 (Accession NM\_032892). Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14161. LOC115330 (Accession NM\_138445) is another VGAM1696 host target gene. LOC115330 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115330, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115330 BINDING SITE, designated SEQ ID:28810, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57157] Another function of VGAM1696 is therefore inhibition of LOC115330 (Accession NM\_138445). Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115330. LOC116437 (Accession XM\_058185) is another VGAM1696 host target gene. LOC116437 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC116437 BINDING SITE, designated SEQ ID:36581, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57158] Another function of VGAM1696 is therefore inhibition of LOC116437 (Accession XM\_058185). Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116437. LOC131873 (Accession XM\_067585) is another VGAM1696 host target gene. LOC131873 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC131873, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131873 BINDING SITE, designated SEQ ID:37366, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57159] Another function of VGAM1696 is therefore inhibition of LOC131873 (Accession XM\_067585). Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131873. LOC58489 (Accession XM\_051862) is an-

other VGAM1696 host target gene. LOC58489 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC58489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58489 BINDING SITE, designated SEQ ID:35907, to the nucleotide sequence of VGAM1696 RNA, herein designated VGAM RNA, also designated SEQ ID:4407.

[57160] Another function of VGAM1696 is therefore inhibition of LOC58489 (Accession XM\_051862). Accordingly, utilities of VGAM1696 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58489. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1697 (VGAM1697) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57161] VGAM1697 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1697 was detected is de-



scribed hereinabove with reference to Figs. 1–8.

[57162] VGAM1697 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1697 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57163] VGAM1697 gene encodes a VGAM1697 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1697 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1697 precursor RNA is designated SEQ ID:1683, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1683 is located at position 50957 relative to the genome of Ectocarpus Siliculosus Virus.

[57164] VGAM1697 precursor RNA folds onto itself, forming VGAM1697 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57165] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1697 folded precursor RNA into VGAM1697 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1697 RNA is designated SEQ ID:4408, and is provided hereinbelow with reference to the sequence listing part.

[57166] VGAM1697 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1697 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1697 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57167] VGAM1697 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1697 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1697 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1697 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1697 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57168] The complementary binding of VGAM1697 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1697 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1697 host target RNA into VGAM1697 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57169] It is appreciated that VGAM1697 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1697 host target genes. The mRNA of each one of this plurality of VGAM1697 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1697 RNA, herein designated VGAM RNA, and which when bound by VGAM1697 RNA causes inhibition of translation of respective one or more VGAM1697 host target proteins.

[57170] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1697 gene, herein designated VGAM GENE, on one or more VGAM1697 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57171] It is yet further appreciated that a function of VGAM1697 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1697 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1697 correlate with, and may be deduced from, the identity of the host target genes which VGAM1697 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57172] Nucleotide sequences of the VGAM1697 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1697 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1697 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1697 are further described hereinbelow with reference to Table 1.

[57173] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1697 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1697 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57174] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1697 gene, herein designated VGAM is inhibition of expression of VGAM1697 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1697 correlate with, and may be deduced from, the identity of the target genes which VGAM1697 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57175] Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM\_096169) is a VGAM1697 host target gene. INPP5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INPP5D, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5D BINDING SITE, designated SEQ ID:40302, to the nucleotide sequence of VGAM1697 RNA, herein designated VGAM RNA, also designated SEQ ID:4408.

[57176] A function of VGAM1697 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM\_096169), a gene which hydrolyzes Ins(1,3,4,5)P<sub>4</sub> and PtdIns(3,4,5)P<sub>3</sub>; contains an SH2-domain. Accordingly, utilities of VGAM1697 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5D. The function of INPP5D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM64. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1698 (VGAM1698) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57177] VGAM1698 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1698 was detected is described hereinabove with reference to Figs. 1–8.

[57178] VGAM1698 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1698 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57179] VGAM1698 gene encodes a VGAM1698 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1698 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1698 precursor RNA is designated SEQ ID:1684, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1684 is located at position 52499 relative to the genome of Ectocarpus Siliculosus Virus.

[57180] VGAM1698 precursor RNA folds onto itself, forming VGAM1698 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by



miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57181] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1698 folded precursor RNA into VGAM1698 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1698 RNA is designated SEQ ID:4409, and is provided hereinbelow with reference to the sequence listing part.

[57182] VGAM1698 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1698 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1698 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57183] VGAM1698 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1698 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1698 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1698 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1698 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57184] The complementary binding of VGAM1698 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1698 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1698 host target RNA into VGAM1698 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57185] It is appreciated that VGAM1698 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1698 host target genes. The mRNA of each one of this plurality of VGAM1698 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1698 RNA, herein designated VGAM RNA, and which when bound by VGAM1698 RNA causes inhibition of translation of respective one or more VGAM1698 host target proteins.

[57186] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1698 gene, herein designated VGAM GENE, on one or more VGAM1698 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57187] It is yet further appreciated that a function of VGAM1698 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1698 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1698 correlate with, and may be deduced from, the identity of the host target genes which VGAM1698 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57188] Nucleotide sequences of the VGAM1698 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1698 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1698 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1698 are further described hereinbelow with reference to Table 1.

[57189] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1698 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1698 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57190] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1698 gene, herein designated VGAM is inhibition of expression of VGAM1698 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1698 correlate with, and may be deduced from, the identity of the target genes which VGAM1698 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57191] KIAA1126 (Accession XM\_050325) is a VGAM1698 host target gene. KIAA1126 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by KIAA1126, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1126 BINDING SITE, designated SEQ ID:35605, to the nucleotide sequence of VGAM1698 RNA, herein designated VGAM RNA, also designated SEQ ID:4409.

[57192] A function of VGAM1698 is therefore inhibition of KIAA1126 (Accession XM\_050325). Accordingly, utilities of VGAM1698 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1126. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1699 (VGAM1699) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57193] VGAM1699 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1699 was detected is described hereinabove with reference to Figs. 1-8.

[57194] VGAM1699 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1699 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57195] VGAM1699 gene encodes a VGAM1699 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1699 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1699 precursor RNA is designated SEQ ID:1685, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1685 is located at position 53142 relative to the genome of Ectocarpus Siliculosus Virus.

[57196] VGAM1699 precursor RNA folds onto itself, forming VGAM1699 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57197] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1699 folded precursor RNA into VGAM1699 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1699 RNA is designated SEQ ID:4410, and is provided hereinbelow with reference to the sequence listing part.

[57198] VGAM1699 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1699 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1699 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57199] VGAM1699 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1699 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM1699 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1699 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1699 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57200] The complementary binding of VGAM1699 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1699 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1699

host target RNA into VGAM1699 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57201] It is appreciated that VGAM1699 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1699 host target genes. The mRNA of each one of this plurality of VGAM1699 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1699 RNA, herein designated VGAM RNA, and which when bound by VGAM1699 RNA causes inhibition of translation of respective one or more VGAM1699 host target proteins.

[57202] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1699 gene, herein designated VGAM GENE, on one or more VGAM1699 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57203] It is yet further appreciated that a function of VGAM1699 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1699 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1699 correlate with, and may be deduced from, the identity of the host target genes which VGAM1699 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57204] Nucleotide sequences of the VGAM1699 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1699 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1699 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1699 are further

described hereinbelow with reference to Table 1.

[57205] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1699 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1699 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57206] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1699 gene, herein designated VGAM is inhibition of expression of VGAM1699 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1699 correlate with, and may be deduced from, the identity of the target genes which VGAM1699 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57207] Hippocalcin-like 1 (HPCAL1, Accession NM\_002149) is a VGAM1699 host target gene. HPCAL1 BINDING SITE1 and HPCAL1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HPCAL1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of HPCAL1 BINDING SITE1 and HPCAL1 BINDING SITE2, designated SEQ ID:7926 and SEQ ID:28633 respectively, to the nucleotide sequence of VGAM1699 RNA, herein designated VGAM RNA, also designated SEQ ID:4410.

[57208] A function of VGAM1699 is therefore inhibition of Hippocalcin-like 1 (HPCAL1, Accession NM\_002149). Accordingly, utilities of VGAM1699 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPCAL1. FLJ11712 (Accession NM\_024570) is another VGAM1699 host target gene. FLJ11712 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11712, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11712 BINDING SITE, designated SEQ ID:23795, to the nucleotide sequence of VGAM1699 RNA, herein designated VGAM RNA, also designated SEQ ID:4410.

[57209] Another function of VGAM1699 is therefore inhibition of FLJ11712 (Accession NM\_024570). Accordingly, utilities of VGAM1699 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ11712. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1700 (VGAM1700) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57210] VGAM1700 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1700 was detected is described hereinabove with reference to Figs. 1–8.

[57211] VGAM1700 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1700 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57212] VGAM1700 gene encodes a VGAM1700 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1700 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1700 precursor RNA is designated SEQ ID:1686, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1686 is located at position 54256 relative to the genome of Ectocarpus Siliculosus Virus.

- [57213] VGAM1700 precursor RNA folds onto itself, forming VGAM1700 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [57214] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1700 folded precursor RNA into VGAM1700 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide sequence of VGAM1700 RNA is designated SEQ ID:4411, and is provided hereinbelow with reference to the sequence listing part.

[57215] VGAM1700 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1700 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1700 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57216] VGAM1700 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1700 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1700 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1700 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in



untranslated regions of a VGAM1700 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57217] The complementary binding of VGAM1700 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1700 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1700 host target RNA into VGAM1700 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57218] It is appreciated that VGAM1700 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1700 host target genes. The mRNA of each one of this plurality of VGAM1700 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1700 RNA, herein designated VGAM RNA, and which when bound by VGAM1700 RNA causes

inhibition of translation of respective one or more VGAM1700 host target proteins.

[57219] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1700 gene, herein designated VGAM GENE, on one or more VGAM1700 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57220] It is yet further appreciated that a function of VGAM1700 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1700 include diagnosis, prevention and

treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1700 correlate with, and may be deduced from, the identity of the host target genes which VGAM1700 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57221] Nucleotide sequences of the VGAM1700 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1700 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1700 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1700 are further described hereinbelow with reference to Table 1.

[57222] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1700 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1700 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57223] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1700 gene, herein designated VGAM is inhibition of expression of VGAM1700 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1700 correlate with, and may be deduced from, the identity of the target genes which VGAM1700 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57224] RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM\_134422) is a VGAM1700 host target gene. RAD52 BINDING SITE1 through RAD52 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD52, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD52 BINDING SITE1 through RAD52 BINDING SITE3, designated SEQ ID:28640, SEQ ID:28650 and SEQ ID:28659 respectively, to the nucleotide sequence of VGAM1700 RNA, herein designated VGAM RNA, also designated SEQ ID:4411.

[57225] A function of VGAM1700 is therefore inhibition of RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM\_134422). Accordingly, utilities of VGAM1700 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD52. FLJ21106 (Accession NM\_025097) is another VGAM1700 host target gene.

FLJ21106 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21106 BINDING SITE, designated SEQ ID:24732, to the nucleotide sequence of VGAM1700 RNA, herein designated VGAM RNA, also designated SEQ ID:4411.

[57226] Another function of VGAM1700 is therefore inhibition of FLJ21106 (Accession NM\_025097). Accordingly, utilities of VGAM1700 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21106. KIAA0429 (Accession NM\_014751) is another VGAM1700 host target gene. KIAA0429 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0429 BINDING SITE, designated SEQ ID:16462, to the nucleotide sequence of VGAM1700 RNA, herein designated VGAM RNA, also designated SEQ ID:4411.

[57227] Another function of VGAM1700 is therefore inhibition of KIAA0429 (Accession NM\_014751). Accordingly, utilities of VGAM1700 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0429. PORIMIN (Accession NM\_052932) is another VGAM1700 host target gene. PORIMIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PORIMIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PORIMIN BINDING SITE, designated SEQ ID:27489, to the nucleotide sequence of VGAM1700 RNA, herein designated VGAM RNA, also designated SEQ ID:4411.

[57228] Another function of VGAM1700 is therefore inhibition of PORIMIN (Accession NM\_052932). Accordingly, utilities of VGAM1700 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PORIMIN. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1701 (VGAM1701) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[57229] VGAM1701 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1701 was detected is described hereinabove with reference to Figs. 1–8.

[57230] VGAM1701 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1701 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57231] VGAM1701 gene encodes a VGAM1701 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1701 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1701 precursor RNA is designated SEQ ID:1687, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1687 is located at position 53594 relative to the genome of Ectocarpus Siliculosus Virus.

[57232] VGAM1701 precursor RNA folds onto itself, forming VGAM1701 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57233] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1701 folded precursor RNA into VGAM1701 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1701 RNA is designated SEQ ID:4412, and is provided hereinbelow with reference to the sequence listing part.

[57234] VGAM1701 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1701 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1701 host target RNA comprises three regions, as is typical of mRNA of a pro-



tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57235] VGAM1701 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1701 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1701 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1701 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1701 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57236] The complementary binding of VGAM1701 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1701 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1701 host target RNA into VGAM1701 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57237] It is appreciated that VGAM1701 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1701 host target genes. The mRNA of each one of this plurality of VGAM1701 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1701 RNA, herein designated VGAM RNA, and which when bound by VGAM1701 RNA causes inhibition of translation of respective one or more VGAM1701 host target proteins.

[57238] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1701 gene, herein designated VGAM GENE, on one or more VGAM1701 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57239] It is yet further appreciated that a function of VGAM1701 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1701 correlate with, and may be deduced from, the identity of the host target genes which VGAM1701 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[57240] Nucleotide sequences of the VGAM1701 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1701 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1701 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1701 are further described hereinbelow with reference to Table 1.

[57241] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1701 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1701 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57242] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1701 gene, herein designated VGAM is inhibition of expression of VGAM1701 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1701 correlate with, and may be deduced from, the identity of the target genes which VGAM1701 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57243] ALEX2 (Accession NM\_014782) is a VGAM1701 host target gene. ALEX2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ALEX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALEX2 BINDING SITE, designated SEQ ID:16635, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57244] A function of VGAM1701 is therefore inhibition of ALEX2 (Accession NM\_014782), a gene which play a role in tumor suppression, possibly by being involved in the regulation of normal cell growth. Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALEX2. The function of ALEX2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1449.DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide, Y Chromosome (DBY, Accession NM\_004660) is another VGAM1701 host target gene. DBY BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by DBY, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DBY BINDING SITE, designated SEQ ID:11027, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57245] Another function of VGAM1701 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide, Y Chromosome (DBY, Accession NM\_004660), a gene which plays a key role in the spermatogenic process. Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DBY. The function of DBY and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM374. Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224) is another VGAM1701 host target gene. ITPR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ITPR3 BINDING SITE, designated SEQ ID:8000, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57246] Another function of VGAM1701 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224), a gene which may be responsible for calcium release from intracellular stores. Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR3. The function of ITPR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM310. Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A, Accession NM\_004788) is another VGAM1701 host target gene. UBE4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE4A BINDING SITE, designated SEQ ID:11198, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA,

also designated SEQ ID:4412.

[57247] Another function of VGAM1701 is therefore inhibition of Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A, Accession NM\_004788), a gene which binds to the ubiquitin moieties of preformed conjugates and catalyzes ubiquitin chain assembly in conjunction with E1, E2, and E3. Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE4A. The function of UBE4A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60.BTB (POZ) Domain Containing 3 (BTBD3, Accession NM\_014962) is another VGAM1701 host target gene. BTBD3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BTBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTBD3 BINDING SITE, designated SEQ ID:17339, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57248] Another function of VGAM1701 is therefore inhibition of



BTB (POZ) Domain Containing 3 (BTBD3, Accession NM\_014962). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTBD3. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294) is another VGAM1701 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26066, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57249] Another function of VGAM1701 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. DKFZp434C0923 (Accession NM\_017598) is another VGAM1701 host target gene. DKFZp434C0923 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by DKFZp434C0923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434C0923 BINDING SITE, designated SEQ ID:19065, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57250] Another function of VGAM1701 is therefore inhibition of DKFZp434C0923 (Accession NM\_017598). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434C0923. FLJ10292 (Accession NM\_018048) is another VGAM1701 host target gene. FLJ10292 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10292 BINDING SITE, designated SEQ ID:19802, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57251] Another function of VGAM1701 is therefore inhibition of

FLJ10292 (Accession NM\_018048). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10292. FLJ11730 (Accession NM\_022756) is another VGAM1701 host target gene. FLJ11730 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11730, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11730 BINDING SITE, designated SEQ ID:22995, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57252] Another function of VGAM1701 is therefore inhibition of FLJ11730 (Accession NM\_022756). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11730. FLJ21432 (Accession NM\_024551) is another VGAM1701 host target gene. FLJ21432 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ21432 BINDING SITE, designated SEQ ID:23768, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57253] Another function of VGAM1701 is therefore inhibition of FLJ21432 (Accession NM\_024551). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21432. KIAA0450 (Accession NM\_014638) is another VGAM1701 host target gene. KIAA0450 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0450 BINDING SITE, designated SEQ ID:16036, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57254] Another function of VGAM1701 is therefore inhibition of KIAA0450 (Accession NM\_014638). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0450. KIAA0544 (Accession XM\_048119) is another

VGAM1701 host target gene. KIAA0544 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0544, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0544 BINDING SITE, designated SEQ ID:35116, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57255] Another function of VGAM1701 is therefore inhibition of KIAA0544 (Accession XM\_048119). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0544. MGC12966 (Accession NM\_032706) is another VGAM1701 host target gene. MGC12966 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12966, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12966 BINDING SITE, designated SEQ ID:26420, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57256] Another function of VGAM1701 is therefore inhibition of MGC12966 (Accession NM\_032706). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12966. Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession XM\_170929) is another VGAM1701 host target gene. PDE4DIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4DIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4DIP BINDING SITE, designated SEQ ID:45710, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57257] Another function of VGAM1701 is therefore inhibition of Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession XM\_170929). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4DIP. LOC139221 (Accession XM\_066558) is another VGAM1701 host target gene. LOC139221 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC139221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139221 BINDING SITE, designated SEQ ID:37332, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57258] Another function of VGAM1701 is therefore inhibition of LOC139221 (Accession XM\_066558). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139221. LOC146287 (Accession XM\_096967) is another VGAM1701 host target gene. LOC146287 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146287, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146287 BINDING SITE, designated SEQ ID:40690, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57259] Another function of VGAM1701 is therefore inhibition of LOC146287 (Accession XM\_096967). Accordingly, utilities

of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146287. LOC149296 (Accession XM\_086481) is another VGAM1701 host target gene. LOC149296 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149296 BINDING SITE, designated SEQ ID:38696, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57260] Another function of VGAM1701 is therefore inhibition of LOC149296 (Accession XM\_086481). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149296. LOC253461 (Accession XM\_172341) is another VGAM1701 host target gene. LOC253461 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC253461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences



of LOC253461 BINDING SITE, designated SEQ ID:46072, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57261] Another function of VGAM1701 is therefore inhibition of LOC253461 (Accession XM\_172341). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253461. LOC58489 (Accession XM\_051862) is another VGAM1701 host target gene. LOC58489 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC58489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58489 BINDING SITE, designated SEQ ID:35906, to the nucleotide sequence of VGAM1701 RNA, herein designated VGAM RNA, also designated SEQ ID:4412.

[57262] Another function of VGAM1701 is therefore inhibition of LOC58489 (Accession XM\_051862). Accordingly, utilities of VGAM1701 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58489. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1702 (VGAM1702) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57263] VGAM1702 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1702 was detected is described hereinabove with reference to Figs. 1–8.

[57264] VGAM1702 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1702 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57265] VGAM1702 gene encodes a VGAM1702 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1702 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1702 precursor RNA is designated SEQ ID:1688, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1688 is located at position 51117 relative to the

genome of Ectocarpus Siliculosus Virus.

[57266] VGAM1702 precursor RNA folds onto itself, forming VGAM1702 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57267] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1702 folded precursor RNA into VGAM1702 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1702 RNA is designated SEQ ID:4413, and is provided hereinbelow with reference to the sequence listing part.

[57268] VGAM1702 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1702 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1702 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[57269] VGAM1702 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1702 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1702 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1702 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1702 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[57270] The complementary binding of VGAM1702 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1702 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1702 host target RNA into VGAM1702 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57271] It is appreciated that VGAM1702 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1702 host target genes. The mRNA of each one of this plurality of VGAM1702 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1702 RNA, herein designated VGAM RNA, and which when bound by VGAM1702 RNA causes inhibition of translation of respective one or more VGAM1702 host target proteins.

[57272] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1702 gene, herein designated VGAM GENE, on one or more VGAM1702 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57273] It is yet further appreciated that a function of VGAM1702 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1702 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of

VGAM1702 correlate with, and may be deduced from, the identity of the host target genes which VGAM1702 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57274] Nucleotide sequences of the VGAM1702 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1702 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1702 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1702 are further described hereinbelow with reference to Table 1.

[57275] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1702 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1702 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57276] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1702 gene, herein designated VGAM is inhibition of expression of VGAM1702 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1702 correlate with, and may be deduced

from, the identity of the target genes which VGAM1702 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57277] ATPase, H<sup>+</sup> Transporting, Lysosomal 42kDa, V1 Subunit C, Isoform 1 (ATP6V1C1, Accession NM\_001695) is a VGAM1702 host target gene. ATP6V1C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP6V1C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP6V1C1 BINDING SITE, designated SEQ ID:7416, to the nucleotide sequence of VGAM1702 RNA, herein designated VGAM RNA, also designated SEQ ID:4413.

[57278] A function of VGAM1702 is therefore inhibition of ATPase, H<sup>+</sup> Transporting, Lysosomal 42kDa, V1 Subunit C, Isoform 1 (ATP6V1C1, Accession NM\_001695), a gene which is necessary for the assembly of the catalytic sector of the enzyme. Accordingly, utilities of VGAM1702 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP6V1C1. The function of ATP6V1C1 has been established by previous studies. Van Hille et al. (1993) cloned subunit C from a human osteo-



clastoma cDNA library with probes developed by PCR from the bovine cDNA sequence (Nelson et al., 1990). The deduced 382-amino acid human ATP6C protein has a calculated molecular mass of 41,941 Da and shows 99% sequence identity with bovine ATP6C. Northern blot analysis detected ubiquitous and comparable expression of a 1.9-kb transcript and a fainter doublet of 6.0–7.0 kb.

[57279] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57280] Nelson, H.; Mandiyan, S.; Noumi, T.; Moriyama, Y.; Miedel, M. C.; Nelson, N. : Molecular cloning of cDNA encoding the C subunit of H(+)-ATPase from bovine chromaffin granules. J. Biol. Chem. 265: 20390–20393, 1990. ; and

[57281] van Hille, B.; Vanek, M.; Richener, H.; Green, J. R.; Bilbe, G. : Cloning and tissue distribution of subunits C, D, and E of the human vacuolar H(+)-ATPase. Biochem. Biophys. Res. Commu.

[57282] Further studies establishing the function and utilities of ATP6V1C1 are found in John Hopkins OMIM database record ID 603097, and in cited publications numbered 8661–8662 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein

Kinase C, Nu (PRKCN, Accession NM\_005813) is another VGAM1702 host target gene. PRKCN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRKCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKCN BINDING SITE, designated SEQ ID:12401, to the nucleotide sequence of VGAM1702 RNA, herein designated VGAM RNA, also designated SEQ ID:4413.

[57283] Another function of VGAM1702 is therefore inhibition of Protein Kinase C, Nu (PRKCN, Accession NM\_005813). Accordingly, utilities of VGAM1702 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKCN. WAS Protein Family, Member 3 (WASF3, Accession NM\_006646) is another VGAM1702 host target gene. WASF3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by WASF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WASF3 BINDING SITE, designated SEQ ID:13444, to the nucleotide sequence of

VGAM1702 RNA, herein designated VGAM RNA, also designated SEQ ID:4413.

[57284] Another function of VGAM1702 is therefore inhibition of WAS Protein Family, Member 3 (WASF3, Accession NM\_006646), a gene which stimulates actin polymerization. Accordingly, utilities of VGAM1702 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WASF3. The function of WASF3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1692. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294) is another VGAM1702 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26064, to the nucleotide sequence of VGAM1702 RNA, herein designated VGAM RNA, also designated SEQ ID:4413.

[57285] Another function of VGAM1702 is therefore inhibition of

Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294). Accordingly, utilities of VGAM1702 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. FLJ12294 (Accession NM\_025100) is another VGAM1702 host target gene. FLJ12294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12294 BINDING SITE, designated SEQ ID:24747, to the nucleotide sequence of VGAM1702 RNA, herein designated VGAM RNA, also designated SEQ ID:4413.

[57286] Another function of VGAM1702 is therefore inhibition of FLJ12294 (Accession NM\_025100). Accordingly, utilities of VGAM1702 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12294. FLJ23598 (Accession XM\_170689) is another VGAM1702 host target gene. FLJ23598 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23598 BINDING SITE, designated SEQ ID:45467, to the nucleotide sequence of VGAM1702 RNA, herein designated VGAM RNA, also designated SEQ ID:4413.

[57287] Another function of VGAM1702 is therefore inhibition of FLJ23598 (Accession XM\_170689). Accordingly, utilities of VGAM1702 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23598. T-box 4 (TBX4, Accession NM\_018488) is another VGAM1702 host target gene. TBX4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBX4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBX4 BINDING SITE, designated SEQ ID:20547, to the nucleotide sequence of VGAM1702 RNA, herein designated VGAM RNA, also designated SEQ ID:4413.

[57288] Another function of VGAM1702 is therefore inhibition of T-box 4 (TBX4, Accession NM\_018488). Accordingly, utilities of VGAM1702 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with TBX4. LOC148147 (Accession XM\_086071) is another VGAM1702 host target gene. LOC148147 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148147, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148147 BINDING SITE, designated SEQ ID:38475, to the nucleotide sequence of VGAM1702 RNA, herein designated VGAM RNA, also designated SEQ ID:4413.

[57289] Another function of VGAM1702 is therefore inhibition of LOC148147 (Accession XM\_086071). Accordingly, utilities of VGAM1702 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148147. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1703 (VGAM1703) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57290] VGAM1703 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1703 was detected is described hereinabove with reference to Figs. 1–8.

[57291] VGAM1703 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1703 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57292] VGAM1703 gene encodes a VGAM1703 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1703 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1703 precursor RNA is designated SEQ ID:1689, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1689 is located at position 53714 relative to the genome of Ectocarpus Siliculosus Virus.

[57293] VGAM1703 precursor RNA folds onto itself, forming VGAM1703 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57294] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1703 folded precursor RNA into VGAM1703 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1703 RNA is designated SEQ ID:4414, and is provided hereinbelow with reference to the sequence listing part.

[57295] VGAM1703 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1703 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1703 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57296] VGAM1703 RNA, herein designated VGAM RNA, binds



complementarily to one or more host target binding sites located in untranslated regions of VGAM1703 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1703 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1703 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1703 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[57297] The complementary binding of VGAM1703 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1703 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1703 host target RNA into VGAM1703 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57298] It is appreciated that VGAM1703 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1703 host target genes. The mRNA of each one of this plurality of VGAM1703 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1703 RNA, herein designated VGAM RNA, and which when bound by VGAM1703 RNA causes inhibition of translation of respective one or more VGAM1703 host target proteins.

[57299] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1703 gene, herein designated VGAM GENE, on one or more VGAM1703 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57300] It is yet further appreciated that a function of VGAM1703 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1703 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1703 correlate with, and may be deduced from, the identity of the host target genes which VGAM1703 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57301] Nucleotide sequences of the VGAM1703 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1703 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1703 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1703 are further described hereinbelow with reference to Table 1.

[57302] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1703 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1703 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57303] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1703 gene, herein designated VGAM is inhibition of expression of VGAM1703 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1703 correlate with, and may be deduced from, the identity of the target genes which VGAM1703 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57304] RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM\_134422) is a VGAM1703 host target gene. RAD52 BINDING SITE1 through RAD52 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of

mRNA encoded by RAD52, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD52 BINDING SITE1 through RAD52 BINDING SITE3, designated SEQ ID:28640, SEQ ID:28650 and SEQ ID:28659 respectively, to the nucleotide sequence of VGAM1703 RNA, herein designated VGAM RNA, also designated SEQ ID:4414.

[57305] A function of VGAM1703 is therefore inhibition of RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM\_134422). Accordingly, utilities of VGAM1703 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD52. ChGn (Accession NM\_018371) is another VGAM1703 host target gene. ChGn BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ChGn, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ChGn BINDING SITE, designated SEQ ID:20390, to the nucleotide sequence of VGAM1703 RNA, herein designated VGAM RNA, also designated SEQ ID:4414.

[57306] Another function of VGAM1703 is therefore inhibition of

ChGn (Accession NM\_018371). Accordingly, utilities of VGAM1703 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ChGn. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1704 (VGAM1704) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57307] VGAM1704 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1704 was detected is described hereinabove with reference to Figs. 1-8.

[57308] VGAM1704 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1704 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57309] VGAM1704 gene encodes a VGAM1704 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1704 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1704 precursor RNA is designated SEQ ID:1690, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1690 is located at position 52170 relative to the genome of Ectocarpus Siliculosus Virus.

- [57310] VGAM1704 precursor RNA folds onto itself, forming VGAM1704 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [57311] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1704 folded precursor RNA into VGAM1704 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1704 RNA is designated SEQ ID:4415, and

is provided hereinbelow with reference to the sequence listing part.

[57312] VGAM1704 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1704 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1704 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[57313] VGAM1704 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1704 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1704 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-



ing – VGAM1704 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1704 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57314] The complementary binding of VGAM1704 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1704 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1704 host target RNA into VGAM1704 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57315] It is appreciated that VGAM1704 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1704 host target genes. The mRNA of each one of this plurality of VGAM1704 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1704 RNA, herein designated VGAM RNA, and which when bound by VGAM1704 RNA causes inhibition of translation of respective one or more VGAM1704 host target proteins.

[57316] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1704 gene, herein designated VGAM GENE, on one or more VGAM1704 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57317] It is yet further appreciated that a function of VGAM1704 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1704 correlate with, and may be deduced from, the identity of the host target genes which VGAM1704 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57318] Nucleotide sequences of the VGAM1704 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1704 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1704 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1704 are further described hereinbelow with reference to Table 1.

[57319] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1704 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1704 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57320] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1704 gene, herein designated VGAM is inhibition of expression of VGAM1704 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1704 correlate with, and may be deduced from, the identity of the target genes which VGAM1704 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57321] Ephrin-B2 (EFNB2, Accession NM\_004093) is a VGAM1704 host target gene. EFNB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNB2 BINDING SITE, designated SEQ ID:10297, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57322] A function of VGAM1704 is therefore inhibition of Ephrin-B2 (EFNB2, Accession NM\_004093). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNB2. Early Growth Response 1 (EGR1, Accession NM\_001964) is another VGAM1704 host target gene.

EGR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGR1 BINDING SITE, designated SEQ ID:7692, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57323] Another function of VGAM1704 is therefore inhibition of Early Growth Response 1 (EGR1, Accession NM\_001964). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGR1. Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM\_002006) is another VGAM1704 host target gene. FGF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF2 BINDING SITE, designated SEQ ID:7744, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57324] Another function of VGAM1704 is therefore inhibition of Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM\_002006), a gene which probably involved in nervous system development and function. Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF2. The function of FGF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51.5–hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868) is another VGAM1704 host target gene. HTR2C BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HTR2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR2C BINDING SITE, designated SEQ ID:6535, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57325] Another function of VGAM1704 is therefore inhibition of 5–hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868), a gene which activates phospho–

lipase C and regulates intracellular calcium flux. Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR2C. The function of HTR2C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1052.

Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224) is another VGAM1704 host target gene.

ITPR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR3 BINDING SITE, designated SEQ ID:7999, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57326] Another function of VGAM1704 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224), a gene which may be responsible for calcium release from intracellular stores. Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with ITPR3. The function of ITPR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM310. Proteasome (prosome, macropain) Subunit, Beta Type, 2 (PSMB2, Accession NM\_002794) is another VGAM1704 host target gene. PSMB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMB2 BINDING SITE, designated SEQ ID:8673, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57327] Another function of VGAM1704 is therefore inhibition of Proteasome (prosome, macropain) Subunit, Beta Type, 2 (PSMB2, Accession NM\_002794). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMB2. Calneuron 1 (CALN1, Accession NM\_031468) is another VGAM1704 host target gene. CALN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALN1, corresponding to a HOST



TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25519, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57328] Another function of VGAM1704 is therefore inhibition of Calneuron 1 (CALN1, Accession NM\_031468). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294) is another VGAM1704 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26068, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57329] Another function of VGAM1704 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1,

Alpha (CAMKK1, Accession NM\_032294). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. DC-TM4F2 (Accession NM\_030927) is another VGAM1704 host target gene. DC-TM4F2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DC-TM4F2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DC-TM4F2 BINDING SITE, designated SEQ ID:25199, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57330] Another function of VGAM1704 is therefore inhibition of DC-TM4F2 (Accession NM\_030927). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DC-TM4F2. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681) is another VGAM1704 host target gene. DDX34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE, designated SEQ ID:16169, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57331] Another function of VGAM1704 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. DRIL2 (Accession NM\_006465) is another VGAM1704 host target gene. DRIL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DRIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRIL2 BINDING SITE, designated SEQ ID:13188, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57332] Another function of VGAM1704 is therefore inhibition of DRIL2 (Accession NM\_006465). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with DRIL2. FLJ12294 (Accession NM\_025100) is another VGAM1704 host target gene. FLJ12294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12294 BINDING SITE, designated SEQ ID:24743, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57333] Another function of VGAM1704 is therefore inhibition of FLJ12294 (Accession NM\_025100). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12294. FLJ13456 (Accession XM\_038291) is another VGAM1704 host target gene. FLJ13456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13456 BINDING SITE, designated SEQ ID:32800, to the nucleotide

sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57334] Another function of VGAM1704 is therefore inhibition of FLJ13456 (Accession XM\_038291). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13456. FLJ20489 (Accession NM\_017842) is another VGAM1704 host target gene. FLJ20489 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20489 BINDING SITE, designated SEQ ID:19507, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57335] Another function of VGAM1704 is therefore inhibition of FLJ20489 (Accession NM\_017842). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20489. FLJ21551 (Accession NM\_024801) is another VGAM1704 host target gene. FLJ21551 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ21551, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21551 BINDING SITE, designated SEQ ID:24181, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57336] Another function of VGAM1704 is therefore inhibition of FLJ21551 (Accession NM\_024801). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21551. FLJ22362 (Accession NM\_022823) is another VGAM1704 host target gene. FLJ22362 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22362 BINDING SITE, designated SEQ ID:23105, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57337] Another function of VGAM1704 is therefore inhibition of FLJ22362 (Accession NM\_022823). Accordingly, utilities of

VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22362. FLJ22692 (Accession NM\_025049) is another VGAM1704 host target gene. FLJ22692 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22692, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22692 BINDING SITE, designated SEQ ID:24644, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57338] Another function of VGAM1704 is therefore inhibition of FLJ22692 (Accession NM\_025049). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22692. FLJ23598 (Accession XM\_170689) is another VGAM1704 host target gene. FLJ23598 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23598

BINDING SITE, designated SEQ ID:45468, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57339] Another function of VGAM1704 is therefore inhibition of FLJ23598 (Accession XM\_170689). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23598. KIAA0795 (Accession NM\_025010) is another VGAM1704 host target gene. KIAA0795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0795 BINDING SITE, designated SEQ ID:24588, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57340] Another function of VGAM1704 is therefore inhibition of KIAA0795 (Accession NM\_025010). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0795. KIAA1872 (Accession XM\_031917) is another VGAM1704 host target gene. KIAA1872 BINDING SITE is



HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1872 BINDING SITE, designated SEQ ID:31518, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57341] Another function of VGAM1704 is therefore inhibition of KIAA1872 (Accession XM\_031917). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1872. LGP1 (Accession NM\_032484) is another VGAM1704 host target gene. LGP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LGP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGP1 BINDING SITE, designated SEQ ID:26232, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57342] Another function of VGAM1704 is therefore inhibition of

LGP1 (Accession NM\_032484). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGP1. Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010) is another VGAM1704 host target gene. MAP2K4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP2K4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K4 BINDING SITE, designated SEQ ID:8917, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57343] Another function of VGAM1704 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K4. MGC29891 (Accession NM\_144618) is another VGAM1704 host target gene. MGC29891 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC29891, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC29891 BINDING SITE, designated SEQ ID:29438, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57344] Another function of VGAM1704 is therefore inhibition of MGC29891 (Accession NM\_144618). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC29891. Nup43 (Accession NM\_024647) is another VGAM1704 host target gene. Nup43 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Nup43, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Nup43 BINDING SITE, designated SEQ ID:23937, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57345] Another function of VGAM1704 is therefore inhibition of Nup43 (Accession NM\_024647). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with Nup43. Neurexophilin 3 (NXPH3, Accession XM\_037847) is another VGAM1704 host target gene. NXPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXPH3 BINDING SITE, designated SEQ ID:32715, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57346] Another function of VGAM1704 is therefore inhibition of Neurexophilin 3 (NXPH3, Accession XM\_037847). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXPH3. Regulator of G-protein Signalling 11 (RGS11, Accession NM\_003834) is another VGAM1704 host target gene. RGS11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGS11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS11 BINDING SITE, des-

ignated SEQ ID:9925, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57347] Another function of VGAM1704 is therefore inhibition of Regulator of G-protein Signalling 11 (RGS11, Accession NM\_003834). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS11. ZAK (Accession NM\_133646) is another VGAM1704 host target gene. ZAK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZAK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZAK BINDING SITE, designated SEQ ID:28606, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57348] Another function of VGAM1704 is therefore inhibition of ZAK (Accession NM\_133646). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZAK. LOC115129 (Accession XM\_055292) is another VGAM1704 host target gene. LOC115129 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115129 BINDING SITE, designated SEQ ID:36255, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57349] Another function of VGAM1704 is therefore inhibition of LOC115129 (Accession XM\_055292). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115129. LOC115330 (Accession NM\_138445) is another VGAM1704 host target gene. LOC115330 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115330, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115330 BINDING SITE, designated SEQ ID:28811, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57350] Another function of VGAM1704 is therefore inhibition of

LOC115330 (Accession NM\_138445). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115330. LOC116437 (Accession XM\_058185) is another VGAM1704 host target gene. LOC116437 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116437 BINDING SITE, designated SEQ ID:36582, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57351] Another function of VGAM1704 is therefore inhibition of LOC116437 (Accession XM\_058185). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116437. LOC145955 (Accession XM\_096912) is another VGAM1704 host target gene. LOC145955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC145955 BINDING SITE, designated SEQ ID:40644, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57352] Another function of VGAM1704 is therefore inhibition of LOC145955 (Accession XM\_096912). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145955. LOC148147 (Accession XM\_086071) is another VGAM1704 host target gene. LOC148147 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148147, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148147 BINDING SITE, designated SEQ ID:38477, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57353] Another function of VGAM1704 is therefore inhibition of LOC148147 (Accession XM\_086071). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148147. LOC149460 (Accession XM\_097652) is an-



other VGAM1704 host target gene. LOC149460 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149460 BINDING SITE, designated SEQ ID:40998, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57354] Another function of VGAM1704 is therefore inhibition of LOC149460 (Accession XM\_097652). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149460. LOC158819 (Accession XM\_098995) is another VGAM1704 host target gene. LOC158819 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158819, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158819 BINDING SITE, designated SEQ ID:42029, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57355] Another function of VGAM1704 is therefore inhibition of LOC158819 (Accession XM\_098995). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158819. LOC169026 (Accession XM\_095471) is another VGAM1704 host target gene. LOC169026 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC169026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169026 BINDING SITE, designated SEQ ID:40269, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57356] Another function of VGAM1704 is therefore inhibition of LOC169026 (Accession XM\_095471). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169026. LOC196955 (Accession XM\_085210) is another VGAM1704 host target gene. LOC196955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196955, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196955 BINDING SITE, designated SEQ ID:37931, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57357] Another function of VGAM1704 is therefore inhibition of LOC196955 (Accession XM\_085210). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196955. LOC199678 (Accession XM\_117111) is another VGAM1704 host target gene. LOC199678 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199678 BINDING SITE, designated SEQ ID:43227, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57358] Another function of VGAM1704 is therefore inhibition of LOC199678 (Accession XM\_117111). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC199678. LOC58489 (Accession XM\_051862) is another VGAM1704 host target gene. LOC58489 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC58489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58489 BINDING SITE, designated SEQ ID:35908, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57359] Another function of VGAM1704 is therefore inhibition of LOC58489 (Accession XM\_051862). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58489. LOC90538 (Accession XM\_032401) is another VGAM1704 host target gene. LOC90538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90538 BINDING SITE, designated SEQ ID:31659, to the nucleotide sequence of VGAM1704 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4415.

[57360] Another function of VGAM1704 is therefore inhibition of LOC90538 (Accession XM\_032401). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90538. LOC93132 (Accession XM\_049396) is another VGAM1704 host target gene. LOC93132 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93132 BINDING SITE, designated SEQ ID:35411, to the nucleotide sequence of VGAM1704 RNA, herein designated VGAM RNA, also designated SEQ ID:4415.

[57361] Another function of VGAM1704 is therefore inhibition of LOC93132 (Accession XM\_049396). Accordingly, utilities of VGAM1704 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93132. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1705 (VGAM1705) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57362] VGAM1705 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1705 was detected is described hereinabove with reference to Figs. 1–8.

[57363] VGAM1705 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1705 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57364] VGAM1705 gene encodes a VGAM1705 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1705 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1705 precursor RNA is designated SEQ ID:1691, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1691 is located at position 51223 relative to the genome of Ectocarpus Siliculosus Virus.

[57365] VGAM1705 precursor RNA folds onto itself, forming

VGAM1705 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57366] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1705 folded precursor RNA into VGAM1705 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1705 RNA is designated SEQ ID:4416, and is provided hereinbelow with reference to the sequence listing part.

[57367] VGAM1705 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1705 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1705 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57368] VGAM1705 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1705 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1705 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1705 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1705 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example



only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57369] The complementary binding of VGAM1705 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1705 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1705 host target RNA into VGAM1705 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57370] It is appreciated that VGAM1705 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1705 host target genes. The mRNA of each one of this plurality of VGAM1705 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1705 RNA, herein designated VGAM RNA, and which when bound by VGAM1705 RNA causes inhibition of translation of respective one or more VGAM1705 host target proteins.

[57371] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1705 gene, herein designated VGAM GENE, on one or more VGAM1705 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57372] It is yet further appreciated that a function of VGAM1705 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1705 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1705 correlate with, and may be deduced from, the identity of the host target genes which VGAM1705 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57373] Nucleotide sequences of the VGAM1705 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1705 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1705 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1705 are further described hereinbelow with reference to Table 1.

[57374] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1705 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1705 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57375] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1705 gene, herein designated VGAM is inhibition of expression of VGAM1705 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1705 correlate with, and may be deduced from, the identity of the target genes which VGAM1705 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[57376] Cystinosis, Nephropathic (CTNS, Accession NM\_004937) is a VGAM1705 host target gene. CTNS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTNS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTNS BINDING SITE, designated SEQ ID:11383, to the nucleotide sequence of VGAM1705 RNA, herein designated VGAM RNA, also designated SEQ ID:4416.

[57377] A function of VGAM1705 is therefore inhibition of Cystinosis, Nephropathic (CTNS, Accession NM\_004937). Accordingly, utilities of VGAM1705 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTNS. Protein Kinase C, Nu (PRKCN, Accession NM\_005813) is another VGAM1705 host target gene. PRKCN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKCN BINDING SITE, designated SEQ

ID:12398, to the nucleotide sequence of VGAM1705 RNA, herein designated VGAM RNA, also designated SEQ ID:4416.

[57378] Another function of VGAM1705 is therefore inhibition of Protein Kinase C, Nu (PRKCN, Accession NM\_005813). Accordingly, utilities of VGAM1705 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKCN. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294) is another VGAM1705 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26065, to the nucleotide sequence of VGAM1705 RNA, herein designated VGAM RNA, also designated SEQ ID:4416.

[57379] Another function of VGAM1705 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294). Accordingly, utilities of VGAM1705 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with CAMKK1. SYNE-2 (Accession NM\_015180) is another VGAM1705 host target gene. SYNE-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNE-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNE-2 BINDING SITE, designated SEQ ID:17535, to the nucleotide sequence of VGAM1705 RNA, herein designated VGAM RNA, also designated SEQ ID:4416.

[57380] Another function of VGAM1705 is therefore inhibition of SYNE-2 (Accession NM\_015180). Accordingly, utilities of VGAM1705 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNE-2. ZF (Accession NM\_021212) is another VGAM1705 host target gene. ZF BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZF BINDING SITE, designated SEQ ID:22189, to the nucleotide sequence of VGAM1705 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4416.

[57381] Another function of VGAM1705 is therefore inhibition of ZF (Accession NM\_021212). Accordingly, utilities of VGAM1705 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZF. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1706 (VGAM1706) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57382] VGAM1706 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1706 was detected is described hereinabove with reference to Figs. 1-8.

[57383] VGAM1706 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1706 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57384] VGAM1706 gene encodes a VGAM1706 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1706 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1706 precursor RNA is designated SEQ ID:1692, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1692 is located at position 54780 relative to the genome of Ectocarpus Siliculosus Virus.

- [57385] VGAM1706 precursor RNA folds onto itself, forming VGAM1706 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [57386] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1706 folded precursor RNA into VGAM1706 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other



necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1706 RNA is designated SEQ ID:4417, and is provided hereinbelow with reference to the sequence listing part.

[57387] VGAM1706 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1706 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1706 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[57388] VGAM1706 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1706 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1706 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1706 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1706 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57389] The complementary binding of VGAM1706 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1706 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1706 host target RNA into VGAM1706 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57390] It is appreciated that VGAM1706 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1706 host target genes. The mRNA of each one of this plurality of VGAM1706 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1706 RNA, herein designated VGAM RNA, and which when bound by VGAM1706 RNA causes inhibition of translation of respective one or more VGAM1706 host target proteins.

[57391] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1706 gene, herein designated VGAM GENE, on one or more VGAM1706 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57392] It is yet further appreciated that a function of VGAM1706 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGAM1706 correlate with, and may be deduced from, the identity of the host target genes which VGAM1706 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57393] Nucleotide sequences of the VGAM1706 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1706 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1706 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1706 are further described hereinbelow with reference to Table 1.

[57394] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1706 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1706 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[57395] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1706 gene, herein designated VGAM is inhibition of expression of VGAM1706 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1706 correlate with, and may be deduced from, the identity of the target genes which VGAM1706 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57396] Ephrin-B2 (EFNB2, Accession NM\_004093) is a VGAM1706 host target gene. EFNB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNB2 BINDING SITE, designated SEQ ID:10297, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57397] A function of VGAM1706 is therefore inhibition of Ephrin-B2 (EFNB2, Accession NM\_004093). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

EFNB2. Early Growth Response 1 (EGR1, Accession NM\_001964) is another VGAM1706 host target gene. EGR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGR1 BINDING SITE, designated SEQ ID:7692, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57398] Another function of VGAM1706 is therefore inhibition of Early Growth Response 1 (EGR1, Accession NM\_001964). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGR1. Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM\_002006) is another VGAM1706 host target gene. FGF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF2 BINDING SITE, designated SEQ ID:7744, to the nucleotide sequence of

VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57399] Another function of VGAM1706 is therefore inhibition of Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM\_002006), a gene which probably involved in nervous system development and function. Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF2. The function of FGF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51.5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868) is another VGAM1706 host target gene. HTR2C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HTR2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR2C BINDING SITE, designated SEQ ID:6535, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57400] Another function of VGAM1706 is therefore inhibition of

5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868), a gene which activates phospholipase C and regulates intracellular calcium flux. Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR2C. The function of HTR2C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1052.

Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224) is another VGAM1706 host target gene.

ITPR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR3 BINDING SITE, designated SEQ ID:7999, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57401] Another function of VGAM1706 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224), a gene which may be responsible for calcium release from intracellular stores. Accordingly,



utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR3. The function of ITPR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM310. Proteasome (prosome, macropain) Subunit, Beta Type, 2 (PSMB2, Accession NM\_002794) is another VGAM1706 host target gene. PSMB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMB2 BINDING SITE, designated SEQ ID:8673, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57402] Another function of VGAM1706 is therefore inhibition of Proteasome (prosome, macropain) Subunit, Beta Type, 2 (PSMB2, Accession NM\_002794). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMB2. Calneuron 1 (CALN1, Accession NM\_031468) is another VGAM1706 host target gene. CALN1 BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25519, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57403] Another function of VGAM1706 is therefore inhibition of Calneuron 1 (CALN1, Accession NM\_031468). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294) is another VGAM1706 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26068, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57404] Another function of VGAM1706 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. DC-TM4F2 (Accession NM\_030927) is another VGAM1706 host target gene. DC-TM4F2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DC-TM4F2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DC-TM4F2 BINDING SITE, designated SEQ ID:25199, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57405] Another function of VGAM1706 is therefore inhibition of DC-TM4F2 (Accession NM\_030927). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DC-TM4F2. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681) is another VGAM1706 host target gene. DDX34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by DDX34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE, designated SEQ ID:16169, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57406] Another function of VGAM1706 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. DRIL2 (Accession NM\_006465) is another VGAM1706 host target gene. DRIL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DRIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRIL2 BINDING SITE, designated SEQ ID:13188, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57407] Another function of VGAM1706 is therefore inhibition of

DRIL2 (Accession NM\_006465). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRIL2. FLJ12294 (Accession NM\_025100) is another VGAM1706 host target gene. FLJ12294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12294 BINDING SITE, designated SEQ ID:24743, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57408] Another function of VGAM1706 is therefore inhibition of FLJ12294 (Accession NM\_025100). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12294. FLJ13456 (Accession XM\_038291) is another VGAM1706 host target gene. FLJ13456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ13456 BINDING SITE, designated SEQ ID:32800, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57409] Another function of VGAM1706 is therefore inhibition of FLJ13456 (Accession XM\_038291). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13456. FLJ20489 (Accession NM\_017842) is another VGAM1706 host target gene. FLJ20489 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20489 BINDING SITE, designated SEQ ID:19507, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57410] Another function of VGAM1706 is therefore inhibition of FLJ20489 (Accession NM\_017842). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20489. FLJ21551 (Accession NM\_024801) is another

VGAM1706 host target gene. FLJ21551 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21551, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21551 BINDING SITE, designated SEQ ID:24181, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57411] Another function of VGAM1706 is therefore inhibition of FLJ21551 (Accession NM\_024801). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21551. FLJ22362 (Accession NM\_022823) is another VGAM1706 host target gene. FLJ22362 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22362 BINDING SITE, designated SEQ ID:23105, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57412] Another function of VGAM1706 is therefore inhibition of FLJ22362 (Accession NM\_022823). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22362. FLJ22692 (Accession NM\_025049) is another VGAM1706 host target gene. FLJ22692 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22692, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22692 BINDING SITE, designated SEQ ID:24644, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57413] Another function of VGAM1706 is therefore inhibition of FLJ22692 (Accession NM\_025049). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22692. FLJ23598 (Accession XM\_170689) is another VGAM1706 host target gene. FLJ23598 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23598 BINDING SITE, designated SEQ ID:45468, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57414] Another function of VGAM1706 is therefore inhibition of FLJ23598 (Accession XM\_170689). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23598. KIAA0795 (Accession NM\_025010) is another VGAM1706 host target gene. KIAA0795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0795 BINDING SITE, designated SEQ ID:24588, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57415] Another function of VGAM1706 is therefore inhibition of KIAA0795 (Accession NM\_025010). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0795. KIAA1872 (Accession XM\_031917) is another VGAM1706 host target gene. KIAA1872 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1872 BINDING SITE, designated SEQ ID:31518, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57416] Another function of VGAM1706 is therefore inhibition of KIAA1872 (Accession XM\_031917). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1872. LGP1 (Accession NM\_032484) is another VGAM1706 host target gene. LGP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LGP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGP1 BINDING SITE, designated SEQ ID:26232, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4417.

[57417] Another function of VGAM1706 is therefore inhibition of LGP1 (Accession NM\_032484). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGP1. Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010) is another VGAM1706 host target gene. MAP2K4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP2K4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K4 BINDING SITE, designated SEQ ID:8917, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57418] Another function of VGAM1706 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K4. MGC29891 (Accession NM\_144618) is another VGAM1706 host target gene. MGC29891 BINDING SITE is HOST TAR-

GET binding site found in the 3' untranslated region of mRNA encoded by MGC29891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC29891 BINDING SITE, designated SEQ ID:29438, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57419] Another function of VGAM1706 is therefore inhibition of MGC29891 (Accession NM\_144618). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC29891. Nup43 (Accession NM\_024647) is another VGAM1706 host target gene. Nup43 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Nup43, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Nup43 BINDING SITE, designated SEQ ID:23937, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57420] Another function of VGAM1706 is therefore inhibition of

Nup43 (Accession NM\_024647). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Nup43. Neurexophilin 3 (NXPH3, Accession XM\_037847) is another VGAM1706 host target gene. NXPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXPH3 BINDING SITE, designated SEQ ID:32715, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57421] Another function of VGAM1706 is therefore inhibition of Neurexophilin 3 (NXPH3, Accession XM\_037847). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXPH3. Regulator of G-protein Signalling 11 (RGS11, Accession NM\_003834) is another VGAM1706 host target gene. RGS11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGS11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS11 BINDING SITE, designated SEQ ID:9925, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57422] Another function of VGAM1706 is therefore inhibition of Regulator of G-protein Signalling 11 (RGS11, Accession NM\_003834). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS11. ZAK (Accession NM\_133646) is another VGAM1706 host target gene. ZAK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZAK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZAK BINDING SITE, designated SEQ ID:28606, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57423] Another function of VGAM1706 is therefore inhibition of ZAK (Accession NM\_133646). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZAK.

LOC115129 (Accession XM\_055292) is another VGAM1706 host target gene. LOC115129 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115129 BINDING SITE, designated SEQ ID:36255, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57424] Another function of VGAM1706 is therefore inhibition of LOC115129 (Accession XM\_055292). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115129. LOC115330 (Accession NM\_138445) is another VGAM1706 host target gene. LOC115330 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115330, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115330 BINDING SITE, designated SEQ ID:28811, to the nucleotide sequence of VGAM1706 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4417.

[57425] Another function of VGAM1706 is therefore inhibition of LOC115330 (Accession NM\_138445). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115330. LOC116437 (Accession XM\_058185) is another VGAM1706 host target gene. LOC116437 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116437 BINDING SITE, designated SEQ ID:36582, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57426] Another function of VGAM1706 is therefore inhibition of LOC116437 (Accession XM\_058185). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116437. LOC145955 (Accession XM\_096912) is another VGAM1706 host target gene. LOC145955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145955, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145955 BINDING SITE, designated SEQ ID:40644, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57427] Another function of VGAM1706 is therefore inhibition of LOC145955 (Accession XM\_096912). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145955. LOC148147 (Accession XM\_086071) is another VGAM1706 host target gene. LOC148147 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148147, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148147 BINDING SITE, designated SEQ ID:38477, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57428] Another function of VGAM1706 is therefore inhibition of LOC148147 (Accession XM\_086071). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC148147. LOC149460 (Accession XM\_097652) is another VGAM1706 host target gene. LOC149460 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149460 BINDING SITE, designated SEQ ID:40998, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57429] Another function of VGAM1706 is therefore inhibition of LOC149460 (Accession XM\_097652). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149460. LOC158819 (Accession XM\_098995) is another VGAM1706 host target gene. LOC158819 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC158819, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158819 BINDING SITE, designated SEQ ID:42029, to

the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57430] Another function of VGAM1706 is therefore inhibition of LOC158819 (Accession XM\_098995). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158819. LOC169026 (Accession XM\_095471) is another VGAM1706 host target gene. LOC169026 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC169026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169026 BINDING SITE, designated SEQ ID:40269, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57431] Another function of VGAM1706 is therefore inhibition of LOC169026 (Accession XM\_095471). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169026. LOC196955 (Accession XM\_085210) is another VGAM1706 host target gene. LOC196955 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC196955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196955 BINDING SITE, designated SEQ ID:37931, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57432] Another function of VGAM1706 is therefore inhibition of LOC196955 (Accession XM\_085210). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196955. LOC199678 (Accession XM\_117111) is another VGAM1706 host target gene. LOC199678 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199678 BINDING SITE, designated SEQ ID:43227, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57433] Another function of VGAM1706 is therefore inhibition of LOC199678 (Accession XM\_117111). Accordingly, utilities

of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199678. LOC58489 (Accession XM\_051862) is another VGAM1706 host target gene. LOC58489 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC58489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58489 BINDING SITE, designated SEQ ID:35908, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57434] Another function of VGAM1706 is therefore inhibition of LOC58489 (Accession XM\_051862). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58489. LOC90538 (Accession XM\_032401) is another VGAM1706 host target gene. LOC90538 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC90538 BINDING SITE, designated SEQ ID:31659, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57435] Another function of VGAM1706 is therefore inhibition of LOC90538 (Accession XM\_032401). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90538. LOC93132 (Accession XM\_049396) is another VGAM1706 host target gene. LOC93132 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93132 BINDING SITE, designated SEQ ID:35411, to the nucleotide sequence of VGAM1706 RNA, herein designated VGAM RNA, also designated SEQ ID:4417.

[57436] Another function of VGAM1706 is therefore inhibition of LOC93132 (Accession XM\_049396). Accordingly, utilities of VGAM1706 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93132. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1707 (VGAM1707) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57437] VGAM1707 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1707 was detected is described hereinabove with reference to Figs. 1–8.

[57438] VGAM1707 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectocarpus Siliculosus Virus. VGAM1707 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57439] VGAM1707 gene encodes a VGAM1707 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1707 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1707 precursor RNA is designated SEQ ID:1693, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1693 is located at position 48576 relative to the

genome of Ectocarpus Siliculosus Virus.

[57440] VGAM1707 precursor RNA folds onto itself, forming VGAM1707 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57441] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1707 folded precursor RNA into VGAM1707 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM1707 RNA is designated SEQ ID:4418, and is provided hereinbelow with reference to the sequence listing part.

[57442] VGAM1707 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1707 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1707 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57443] VGAM1707 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1707 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1707 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1707 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1707 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[57444] The complementary binding of VGAM1707 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1707 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1707 host target RNA into VGAM1707 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57445] It is appreciated that VGAM1707 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1707 host target genes. The mRNA of each one of this plurality of VGAM1707 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1707 RNA, herein designated VGAM RNA, and which when bound by VGAM1707 RNA causes inhibition of translation of respective one or more VGAM1707 host target proteins.

[57446] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1707 gene, herein designated VGAM GENE, on one or more VGAM1707 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57447] It is yet further appreciated that a function of VGAM1707 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of

VGAM1707 correlate with, and may be deduced from, the identity of the host target genes which VGAM1707 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57448] Nucleotide sequences of the VGAM1707 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1707 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1707 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1707 are further described hereinbelow with reference to Table 1.

[57449] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1707 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1707 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57450] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1707 gene, herein designated VGAM is inhibition of expression of VGAM1707 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1707 correlate with, and may be deduced

from, the identity of the target genes which VGAM1707 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57451] Amiloride-sensitive Cation Channel 2, Neuronal (ACCN2, Accession NM\_020039) is a VGAM1707 host target gene. ACCN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ACCN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACCN2 BINDING SITE, designated SEQ ID:21296, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57452] A function of VGAM1707 is therefore inhibition of Amiloride-sensitive Cation Channel 2, Neuronal (ACCN2, Accession NM\_020039). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACCN2. Acetylcholinesterase (YT blood group) (ACHE, Accession NM\_015831) is another VGAM1707 host target gene. ACHE BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ACHE,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACHE BINDING SITE, designated SEQ ID:17943, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57453] Another function of VGAM1707 is therefore inhibition of Acetylcholinesterase (YT blood group) (ACHE, Accession NM\_015831), a gene which rapidly hydrolyzes choline released into the synapse. Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACHE. The function of ACHE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1020. Beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_018644) is another VGAM1707 host target gene. B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GAT1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the comple-

mentarity of the nucleotide sequences of B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2, designated SEQ ID:20717 and SEQ ID:27629 respectively, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57454] Another function of VGAM1707 is therefore inhibition of Beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_018644). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GAT1. G1 to S Phase Transition 1 (GSPT1, Accession NM\_002094) is another VGAM1707 host target gene. GSPT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GSPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GSPT1 BINDING SITE, designated SEQ ID:7882, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57455] Another function of VGAM1707 is therefore inhibition of G1 to S Phase Transition 1 (GSPT1, Accession

NM\_002094), a gene which involves in regulation of mammalian cell growth. Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GSPT1. The function of GSPT1 has been established by previous studies. Kikuchi et al. (1988) isolated a gene from a yeast genomic library that could complement a temperature-sensitive mutant of *Saccharomyces cerevisiae*. The gene, termed GST1, seemed to be essential for the G1-to-S phase transition in the yeast cell cycle. The gene product appeared to be a GTP-binding protein of molecular mass 76,565 Da, with 38% identity in amino acid sequence with the alpha subunit of elongation factor-1 (OMIM Ref. No. 130590). Hoshino et al. (1989) cloned the human equivalent from a cDNA library. By nonradioactive in situ hybridization, Ozawa et al. (1992) mapped the GSPT1 gene, the human homolog of the yeast gene GST1-Hs, to human chromosome 16p13.1. Southern blot hybridization with a panel of human-rodent somatic cells confirmed the localization of the GSPT1 gene on chromosome 16 and also showed the existence of a homologous gene on the X chromosome. They pointed out that a breakpoint for non-random chromosome rearrangements has been found in



the region of GSPT1 in patients with acute nonlymphocytic leukemia.

[57456] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57457] Ozawa, K.; Murakami, Y.; Eki, T.; Yokoyama, K.; Soeda, E.; Hoshino, S.; Ui, M.; Hanaoka, F. : Mapping of the human GSPT1 gene, a human homolog of the yeast GST1 gene, to chromosomal band 16p13.1. Somat. Cell Molec. Genet. 18: 189–194, 1992. ; and

[57458] Hoshino, S.; Miyazawa, H.; Enomoto, T.; Hanaoka, F.; Kikuchi, Y.; Kikuchi, A.; Ui, M. : A human homologue of the yeast GST1 gene codes for a GTP-binding protein and is expressed in a pro.

[57459] Further studies establishing the function and utilities of GSPT1 are found in John Hopkins OMIM database record ID 139259, and in cited publications numbered 1883–1885 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Potassium Channel, Subfamily K, Member 4 (KCNK4, Accession NM\_016611) is another VGAM1707 host target gene. KCNK4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

KCNK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNK4 BINDING SITE, designated SEQ ID:18715, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57460] Another function of VGAM1707 is therefore inhibition of Potassium Channel, Subfamily K, Member 4 (KCNK4, Accession NM\_016611). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNK4. KIP2 (Accession NM\_006383) is another VGAM1707 host target gene. KIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIP2 BINDING SITE, designated SEQ ID:13088, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57461] Another function of VGAM1707 is therefore inhibition of KIP2 (Accession NM\_006383). Accordingly, utilities of

VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIP2. Mel Transforming Oncogene (derived from cell line NK14)– RAB8 Homolog (MEL, Accession NM\_005370) is another VGAM1707 host target gene. MEL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEL BINDING SITE, designated SEQ ID:11844, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57462] Another function of VGAM1707 is therefore inhibition of Mel Transforming Oncogene (derived from cell line NK14)– RAB8 Homolog (MEL, Accession NM\_005370), a gene which may be involved in vesicular trafficking and neurotransmitter release. Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEL. The function of MEL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM40.Matrix Metalloproteinase 15

(membrane-inserted) (MMP15, Accession NM\_002428) is another VGAM1707 host target gene. MMP15 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MMP15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP15 BINDING SITE, designated SEQ ID:8262, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57463] Another function of VGAM1707 is therefore inhibition of Matrix Metalloproteinase 15 (membrane-inserted) (MMP15, Accession NM\_002428). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP15. Neurogranin (protein kinase C substrate, RC3) (NRGN, Accession NM\_006176) is another VGAM1707 host target gene. NRGN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NRGN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of NRGN BINDING SITE, designated SEQ ID:12836, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57464] Another function of VGAM1707 is therefore inhibition of Neurogranin (protein kinase C substrate, RC3) (NRGN, Accession NM\_006176), a gene which acts as a "third messenger" substrate of protein kinase c-mediated molecular cascades during synaptic development and remodeling. Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRGN. The function of NRGN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1677. Neurexin 2 (NRXN2, Accession NM\_015080) is another VGAM1707 host target gene. NRXN2 BINDING SITE1 through NRXN2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NRXN2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRXN2 BINDING SITE1 through NRXN2 BINDING SITE3,

designated SEQ ID:17467, SEQ ID:28983 and SEQ ID:28989 respectively, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57465] Another function of VGAM1707 is therefore inhibition of Neurexin 2 (NRXN2, Accession NM\_015080), a gene which may be involved in cell recognition, cell adhesion, and may mediate intracellular signaling. Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRXN2. The function of NRXN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM\_005063) is another VGAM1707 host target gene. SCD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCD BINDING SITE, designated SEQ ID:11496, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA,

also designated SEQ ID:4418.

[57466] Another function of VGAM1707 is therefore inhibition of Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM\_005063), a gene which functions in the synthesis of unsaturated fatty acids. Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCD. The function of SCD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM314. Staufen, RNA Binding Protein (Drosophila) (STAU, Accession NM\_004602) is another VGAM1707 host target gene. STAU BINDING SITE1 through STAU BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by STAU, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAU BINDING SITE1 through STAU BINDING SITE4, designated SEQ ID:10944, SEQ ID:18928, SEQ ID:18916 and SEQ ID:18922 respectively, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57467] Another function of VGAM1707 is therefore inhibition of Staufen, RNA Binding Protein (Drosophila) (STAU, Accession NM\_004602), a gene which may play a role in specific positioning of mrnas at given sites in the cell and in stimulating their translation at the site. Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAU. The function of STAU and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM916. Transcription Factor Binding to IGHM Enhancer 3 (TFE3, Accession NM\_006521) is another VGAM1707 host target gene. TFE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFE3 BINDING SITE, designated SEQ ID:13276, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57468] Another function of VGAM1707 is therefore inhibition of Transcription Factor Binding to IGHM Enhancer 3 (TFE3,



Accession NM\_006521), a gene which is a positive-acting transcription factor that binds to the immunoglobulin enhancer  $\mu$ 3 motif. Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFE3. The function of TFE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM443. Chromosome 1 Open Reading Frame 2 (C1orf2, Accession NM\_006589) is another VGAM1707 host target gene. C1orf2 BINDING SITE1 and C1orf2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by C1orf2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf2 BINDING SITE1 and C1orf2 BINDING SITE2, designated SEQ ID:13355 and SEQ ID:45395 respectively, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57469] Another function of VGAM1707 is therefore inhibition of Chromosome 1 Open Reading Frame 2 (C1orf2, Accession NM\_006589). Accordingly, utilities of VGAM1707 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf2. Centaurin, Beta 5 (CENTB5, Accession XM\_170937) is another VGAM1707 host target gene. CENTB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTB5 BINDING SITE, designated SEQ ID:45726, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57470] Another function of VGAM1707 is therefore inhibition of Centaurin, Beta 5 (CENTB5, Accession XM\_170937). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTB5. Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM\_004273) is another VGAM1707 host target gene. CHST3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CHST3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of CHST3 BINDING SITE, designated SEQ ID:10479, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57471] Another function of VGAM1707 is therefore inhibition of Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM\_004273). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST3. DKFZP586M1120 (Accession NM\_031294) is another VGAM1707 host target gene. DKFZP586M1120 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586M1120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586M1120 BINDING SITE, designated SEQ ID:25319, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57472] Another function of VGAM1707 is therefore inhibition of DKFZP586M1120 (Accession NM\_031294). Accordingly, utilities of VGAM1707 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP586M1120. Fatty Acid Desaturase 1 (FADS1, Accession NM\_013402) is another VGAM1707 host target gene. FADS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FADS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FADS1 BINDING SITE, designated SEQ ID:15068, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57473] Another function of VGAM1707 is therefore inhibition of Fatty Acid Desaturase 1 (FADS1, Accession NM\_013402). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FADS1. FLJ13310 (Accession NM\_025118) is another VGAM1707 host target gene. FLJ13310 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of FLJ13310 BINDING SITE, designated SEQ ID:24767, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57474] Another function of VGAM1707 is therefore inhibition of FLJ13310 (Accession NM\_025118). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13310. FLJ14251 (Accession NM\_024881) is another VGAM1707 host target gene. FLJ14251 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14251 BINDING SITE, designated SEQ ID:24326, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57475] Another function of VGAM1707 is therefore inhibition of FLJ14251 (Accession NM\_024881). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14251. FLJ21839 (Accession NM\_021831) is another

VGAM1707 host target gene. FLJ21839 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21839, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21839 BINDING SITE, designated SEQ ID:22406, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57476] Another function of VGAM1707 is therefore inhibition of FLJ21839 (Accession NM\_021831). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21839. HRD1 (Accession XM\_045498) is another VGAM1707 host target gene. HRD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRD1 BINDING SITE, designated SEQ ID:34470, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57477] Another function of VGAM1707 is therefore inhibition of HRD1 (Accession XM\_045498). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRD1. HU-K4 (Accession NM\_012268) is another VGAM1707 host target gene. HU-K4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HU-K4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HU-K4 BINDING SITE, designated SEQ ID:14590, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57478] Another function of VGAM1707 is therefore inhibition of HU-K4 (Accession NM\_012268). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HU-K4. KIAA0082 (Accession XM\_166400) is another VGAM1707 host target gene. KIAA0082 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0082 BINDING SITE, designated SEQ ID:44263, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57479] Another function of VGAM1707 is therefore inhibition of KIAA0082 (Accession XM\_166400). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0082. KIAA0429 (Accession NM\_014751) is another VGAM1707 host target gene. KIAA0429 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0429 BINDING SITE, designated SEQ ID:16468, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57480] Another function of VGAM1707 is therefore inhibition of KIAA0429 (Accession NM\_014751). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



KIAA0429. KIAA1240 (Accession XM\_039676) is another VGAM1707 host target gene. KIAA1240 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1240, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1240 BINDING SITE, designated SEQ ID:33142, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57481] Another function of VGAM1707 is therefore inhibition of KIAA1240 (Accession XM\_039676). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1240. KIAA1719 (Accession XM\_042936) is another VGAM1707 host target gene. KIAA1719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33817, to the nucleotide sequence of VGAM1707 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4418.

[57482] Another function of VGAM1707 is therefore inhibition of KIAA1719 (Accession XM\_042936). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. KIAA1854 (Accession XM\_049884) is another VGAM1707 host target gene. KIAA1854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35528, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57483] Another function of VGAM1707 is therefore inhibition of KIAA1854 (Accession XM\_049884). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. KIAA1855 (Accession XM\_166453) is another VGAM1707 host target gene. KIAA1855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1855, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1855 BINDING SITE, designated SEQ ID:44354, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57484] Another function of VGAM1707 is therefore inhibition of KIAA1855 (Accession XM\_166453). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1855. MGC4796 (Accession XM\_029031) is another VGAM1707 host target gene. MGC4796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4796 BINDING SITE, designated SEQ ID:30834, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57485] Another function of VGAM1707 is therefore inhibition of MGC4796 (Accession XM\_029031). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC4796. NET-7 (Accession NM\_012339) is another VGAM1707 host target gene. NET-7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NET-7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NET-7 BINDING SITE, designated SEQ ID:14735, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57486] Another function of VGAM1707 is therefore inhibition of NET-7 (Accession NM\_012339). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NET-7. Protein Kinase, Lysine Deficient 2 (PRKWINK2, Accession XM\_117531) is another VGAM1707 host target gene. PRKWINK2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRKWINK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKWINK2 BINDING SITE, designated SEQ

ID:43517, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57487] Another function of VGAM1707 is therefore inhibition of Protein Kinase, Lysine Deficient 2 (PRKWNK2, Accession XM\_117531). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKWNK2. Septin 3 (SEPT3, Accession NM\_019106) is another VGAM1707 host target gene. SEPT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEPT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPT3 BINDING SITE, designated SEQ ID:21183, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57488] Another function of VGAM1707 is therefore inhibition of Septin 3 (SEPT3, Accession NM\_019106). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPT3. LOC114932 (Accession XM\_052614) is an–

other VGAM1707 host target gene. LOC114932 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC114932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114932 BINDING SITE, designated SEQ ID:36008, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57489] Another function of VGAM1707 is therefore inhibition of LOC114932 (Accession XM\_052614). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114932. LOC115708 (Accession XM\_056552) is another VGAM1707 host target gene. LOC115708 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115708, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115708 BINDING SITE, designated SEQ ID:36404, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57490] Another function of VGAM1707 is therefore inhibition of LOC115708 (Accession XM\_056552). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115708. LOC131034 (Accession NM\_130808) is another VGAM1707 host target gene. LOC131034 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC131034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131034 BINDING SITE, designated SEQ ID:28315, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57491] Another function of VGAM1707 is therefore inhibition of LOC131034 (Accession NM\_130808). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131034. LOC145082 (Accession XM\_096719) is another VGAM1707 host target gene. LOC145082 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145082, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145082 BINDING SITE, designated SEQ ID:40493, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57492] Another function of VGAM1707 is therefore inhibition of LOC145082 (Accession XM\_096719). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145082. LOC145371 (Accession XM\_085123) is another VGAM1707 host target gene. LOC145371 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145371 BINDING SITE, designated SEQ ID:37844, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57493] Another function of VGAM1707 is therefore inhibition of LOC145371 (Accession XM\_085123). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC145371. LOC146268 (Accession XM\_085397) is another VGAM1707 host target gene. LOC146268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146268 BINDING SITE, designated SEQ ID:38121, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57494] Another function of VGAM1707 is therefore inhibition of LOC146268 (Accession XM\_085397). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146268. LOC148530 (Accession XM\_097480) is another VGAM1707 host target gene. LOC148530 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148530, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148530 BINDING SITE, designated SEQ ID:40888, to the nucleotide sequence of VGAM1707 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4418.

[57495] Another function of VGAM1707 is therefore inhibition of LOC148530 (Accession XM\_097480). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148530. LOC150538 (Accession XM\_086945) is another VGAM1707 host target gene. LOC150538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150538 BINDING SITE, designated SEQ ID:38990, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57496] Another function of VGAM1707 is therefore inhibition of LOC150538 (Accession XM\_086945). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150538. LOC157922 (Accession XM\_098841) is another VGAM1707 host target gene. LOC157922 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157922, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157922 BINDING SITE, designated SEQ ID:41891, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57497] Another function of VGAM1707 is therefore inhibition of LOC157922 (Accession XM\_098841). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157922. LOC158722 (Accession XM\_088653) is another VGAM1707 host target gene. LOC158722 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158722, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158722 BINDING SITE, designated SEQ ID:39890, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57498] Another function of VGAM1707 is therefore inhibition of LOC158722 (Accession XM\_088653). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC158722. LOC162083 (Accession XM\_091339) is another VGAM1707 host target gene. LOC162083 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC162083, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162083 BINDING SITE, designated SEQ ID:40048, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57499] Another function of VGAM1707 is therefore inhibition of LOC162083 (Accession XM\_091339). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162083. LOC201911 (Accession XM\_117339) is another VGAM1707 host target gene. LOC201911 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC201911, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201911 BINDING SITE, designated SEQ ID:43390, to

the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57500] Another function of VGAM1707 is therefore inhibition of LOC201911 (Accession XM\_117339). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201911. LOC219653 (Accession XM\_166093) is another VGAM1707 host target gene. LOC219653 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219653, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219653 BINDING SITE, designated SEQ ID:43867, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57501] Another function of VGAM1707 is therefore inhibition of LOC219653 (Accession XM\_166093). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219653. LOC221399 (Accession XM\_168134) is another VGAM1707 host target gene. LOC221399 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC221399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221399 BINDING SITE, designated SEQ ID:45048, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57502] Another function of VGAM1707 is therefore inhibition of LOC221399 (Accession XM\_168134). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221399. LOC90271 (Accession XM\_030445) is another VGAM1707 host target gene. LOC90271 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90271 BINDING SITE, designated SEQ ID:31045, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57503] Another function of VGAM1707 is therefore inhibition of LOC90271 (Accession XM\_030445). Accordingly, utilities

of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90271. LOC90550 (Accession XM\_054582) is another VGAM1707 host target gene. LOC90550 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90550, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90550 BINDING SITE, designated SEQ ID:36177, to the nucleotide sequence of VGAM1707 RNA, herein designated VGAM RNA, also designated SEQ ID:4418.

[57504] Another function of VGAM1707 is therefore inhibition of LOC90550 (Accession XM\_054582). Accordingly, utilities of VGAM1707 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90550. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1708 (VGAM1708) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57505] VGAM1708 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1708 was detected is described hereinabove with reference to Figs. 1-8.

[57506] VGAM1708 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Adenovirus B. VGAM1708 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57507] VGAM1708 gene encodes a VGAM1708 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1708 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1708 precursor RNA is designated SEQ ID:1694, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1694 is located at position 17661 relative to the genome of Bovine Adenovirus B.

[57508] VGAM1708 precursor RNA folds onto itself, forming VGAM1708 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the



art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57509] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1708 folded precursor RNA into VGAM1708 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1708 RNA is designated SEQ ID:4419, and is provided hereinbelow with reference to the sequence listing part.

[57510] VGAM1708 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1708 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1708 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[57511] VGAM1708 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1708 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1708 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1708 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1708 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57512] The complementary binding of VGAM1708 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1708 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1708 host target RNA into VGAM1708 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57513] It is appreciated that VGAM1708 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1708 host target genes. The mRNA of each one of this plurality of VGAM1708 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1708 RNA, herein designated VGAM RNA, and which when bound by VGAM1708 RNA causes inhibition of translation of respective one or more VGAM1708 host target proteins.

[57514] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1708 gene, herein designated VGAM GENE, on one or more VGAM1708 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57515] It is yet further appreciated that a function of VGAM1708 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of viral infection by Bovine Adenovirus B. Specific functions, and accordingly utilities, of VGAM1708 correlate with, and may be deduced from, the identity of the host target genes which VGAM1708 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57516] Nucleotide sequences of the VGAM1708 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1708 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1708 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1708 are further  
described hereinbelow with reference to Table 1.

[57517] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1708 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1708 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[57518] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1708 gene, herein designated VGAM is  
inhibition of expression of VGAM1708 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1708 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1708  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[57519] A Disintegrin-like and Metalloprotease (reprolysin type)  
with Thrombospondin Type 1 Motif, 3 (ADAMTS3, Acces-

sion NM\_014243) is a VGAM1708 host target gene.

ADAMTS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAMTS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS3 BINDING SITE, designated SEQ ID:15511, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57520] A function of VGAM1708 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 3 (ADAMTS3, Accession NM\_014243), a gene which cleaves the propeptides of type ii collagen prior to fibril assembly. Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS3. The function of ADAMTS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM211. Apoptotic Protease Activating Factor (APAF1, Accession NM\_013229) is another VGAM1708 host target gene. APAF1 BINDING SITE1

and APAF1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by APAF1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APAF1 BINDING SITE1 and APAF1 BINDING SITE2, designated SEQ ID:14872 and SEQ ID:6833 respectively, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57521] Another function of VGAM1708 is therefore inhibition of Apoptotic Protease Activating Factor (APAF1, Accession NM\_013229), a gene which functions in the mitochondrial apoptotic pathway that leads to caspase 9 dependent activation of caspase 3. Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APAF1. The function of APAF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552.Cerebellar Degeneration-related Protein 2, 62kDa (CDR2, Accession XM\_071866) is another VGAM1708 host target gene. CDR2 BINDING SITE is HOST

TARGET binding site found in the 5` untranslated region of mRNA encoded by CDR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDR2 BINDING SITE, designated SEQ ID:37429, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57522] Another function of VGAM1708 is therefore inhibition of Cerebellar Degeneration-related Protein 2, 62kDa (CDR2, Accession XM\_071866), a gene which plays a role in cytokinesis, cell shape, and functions such as secretion and capping. Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDR2. The function of CDR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128. Dihydropyrimidinase-like 2 (DPYSL2, Accession NM\_001386) is another VGAM1708 host target gene. DPYSL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DPYSL2, corresponding to a HOST TARGET binding site



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPYSL2 BINDING SITE, designated SEQ ID:7067, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57523] Another function of VGAM1708 is therefore inhibition of Dihydropyrimidinase-like 2 (DPYSL2, Accession NM\_001386), a gene which is a member of the dihydropyrimidinase family. Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYSL2. The function of DPYSL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. Phosducin-like (PDCL, Accession NM\_005388) is another VGAM1708 host target gene. PDCL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDCL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDCL BINDING SITE, designated SEQ ID:11867, to the nucleotide

sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57524] Another function of VGAM1708 is therefore inhibition of Phosducin-like (PDCL, Accession NM\_005388), a gene which may regulate G-protein signaling and similar to phosducins. Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDCL. The function of PDCL has been established by previous studies. Phosducin-like protein (PDCL) is a putative modulator of heterotrimeric G proteins. It was initially isolated as the product of an ethanol-responsive gene in neural cell cultures (Miles et al., 1993). PDCL shares extensive amino acid sequence homology with phosducin (PDC; 171490), a phosphoprotein expressed in retina and pineal gland that inhibits several G protein-coupled signaling pathways by binding to the beta-gamma subunits of G proteins. By screening a human genomic library with a rat Pdcl cDNA, Thibault et al. (1999) isolated a partial PDCL genomic sequence. They also identified several PDCL ESTs. The authors derived the complete PDCL coding sequence by aligning the genomic and EST sequences. The predicted 301-amino acid PDCL protein shows homology to areas of rat Pdc that contact G

protein beta-gamma subunits. The N-terminal regions of human, rat, and *Drosophila* PDCL are highly homologous to each other, but show little homology to the N-terminal region of rat Pdc. By somatic cell hybrid analysis, Thibault et al. (1999) mapped the PDCL gene to chromosome 9. Using a radiation hybrid mapping panel, they found that the PDCL gene is linked to markers D9S1876 and D9S1674.

[57525] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57526] Miles, M. F.; Barhite, S.; Sganga, M.; Elliott, M. : Phosducin-like protein: an ethanol-responsive potential modulator of guanine nucleotide-binding protein function. Proc. Nat. Acad. Sci. 90: 10831-10835, 1993. ; and

[57527] Thibault, C.; Wang, J. F.; Charnas, R.; Mirel, D.; Barhite, S.; Miles, M. F. : Cloning and characterization of the rat and human phosducin-like protein genes: structure, expression and.

[57528] Further studies establishing the function and utilities of PDCL are found in John Hopkins OMIM database record ID 604421, and in cited publications numbered 7403-7404 listed in the bibliography section hereinbelow, which are

also hereby incorporated by reference. Requiem, Apoptosis Response Zinc Finger Gene (REQ, Accession NM\_006268) is another VGAM1708 host target gene. REQ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by REQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of REQ BINDING SITE, designated SEQ ID:12953, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57529] Another function of VGAM1708 is therefore inhibition of Requiem, Apoptosis Response Zinc Finger Gene (REQ, Accession NM\_006268), a gene which is a putative zinc finger that is required for apoptosis in murine myeloid cell lines. Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with REQ. The function of REQ and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. Splicing Factor Proline/glutamine Rich (polypyrimidine tract binding protein associated) (SFPQ, Accession NM\_005066) is another

VGAM1708 host target gene. SFPQ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFPQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFPQ BINDING SITE, designated SEQ ID:11505, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57530] Another function of VGAM1708 is therefore inhibition of Splicing Factor Proline/glutamine Rich (polypyrimidine tract binding protein associated) (SFPQ, Accession NM\_005066), a gene which binds intronic polypyrimidine tracts. Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFPQ. The function of SFPQ has been established by previous studies. Patton et al. (1993) identified a 100-kD protein that copurified and associated with polypyrimidine tract-binding protein (PTB; 600693). By microsequence analysis and PCR, followed by screening a fetal brain cDNA library, Patton et al. (1993) isolated cDNAs encoding alternatively spliced isoforms of this protein, which they called PSF (PTB-associated splicing fac-

tor). The deduced 669- and 707-amino acid PSF isoforms contain 2 consensus RNA-binding domains and an unusual N terminus rich in proline and glutamine residues. PSF is highly basic and has a predicted molecular mass of 76 kD, which is much lower than the experimentally determined molecular mass of 100 kD. Northern blot analysis detected PSF transcripts of 2.5 and 3.0 kb, consistent with the alternative splicing. The authors found that the RNA-binding properties of PSF are identical to those of PTB and that both proteins, together and independently, bind the polypyrimidine tract of mammalian introns. Biochemical complementation, antibody inhibition, and immunodepletion experiments demonstrated that PSF is an essential pre-mRNA splicing factor required early in spliceosome formation. Bacterially synthesized PSF was able to complement immunodepleted extracts and restore splicing activity. Despite its association with PSF, complementary experiments with antibodies against PTB did not suggest an essential role for PTB in pre-mRNA splicing. Clark et al. (1997) identified cases of papillary renal cell carcinoma in which the splicing factor gene PSF was partnered with the TFE3 gene as a result of a translocation, t(X;1)(p11.2;p34).

[57531] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57532] Patton, J. G.; Porro, E. B.; Galceran, J.; Tempst, P.; Nadal-Ginard, B. : Cloning and characterization of PSF, a novel pre-mRNA splicing factor. *Genes Dev.* 7: 393–406, 1993. ; and

[57533] Clark, J.; Lu, Y.-J.; Sidhar, S. K.; Parker, C.; Gill, S.; Smedley, D.; Hamoudi, R.; Linehan, W. M.; Shipley, J.; Cooper, C. S. : Fusion of splicing factor genes PSF and NonO (p54-nrb) to.

[57534] Further studies establishing the function and utilities of SFPQ are found in John Hopkins OMIM database record ID 605199, and in cited publications numbered 6610–6611 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nuclear Antigen Sp100 (SP100, Accession NM\_003113) is another VGAM1708 host target gene. SP100 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SP100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP100 BINDING SITE,

designated SEQ ID:9086, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57535] Another function of VGAM1708 is therefore inhibition of Nuclear Antigen Sp100 (SP100, Accession NM\_003113), a gene which may be involved in transduction of interferon action. Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP100. The function of SP100 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM520.Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM\_139177) is another VGAM1708 host target gene. C17orf26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C17orf26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf26 BINDING SITE, designated SEQ ID:29190, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.



[57536] Another function of VGAM1708 is therefore inhibition of Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM\_139177). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf26. Cyclin M1 (CNNM1, Accession NM\_020348) is another VGAM1708 host target gene. CNNM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM1 BINDING SITE, designated SEQ ID:21614, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57537] Another function of VGAM1708 is therefore inhibition of Cyclin M1 (CNNM1, Accession NM\_020348). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM1. DKFZp547O146 (Accession NM\_020224) is another VGAM1708 host target gene. DKFZp547O146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DK-

FZp547O146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547O146 BINDING SITE, designated SEQ ID:21487, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57538] Another function of VGAM1708 is therefore inhibition of DKFZp547O146 (Accession NM\_020224). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547O146. DKFZP564J157 (Accession NM\_018457) is another VGAM1708 host target gene. DKFZP564J157 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564J157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564J157 BINDING SITE, designated SEQ ID:20530, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57539] Another function of VGAM1708 is therefore inhibition of

DKFZP564J157 (Accession NM\_018457). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564J157. DKFZp761K1423 (Accession NM\_018422) is another VGAM1708 host target gene. DKFZp761K1423 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp761K1423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761K1423 BINDING SITE, designated SEQ ID:20476, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57540] Another function of VGAM1708 is therefore inhibition of DKFZp761K1423 (Accession NM\_018422). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761K1423. FLJ20511 (Accession NM\_017853) is another VGAM1708 host target gene. FLJ20511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20511, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20511 BINDING SITE, designated SEQ ID:19531, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57541] Another function of VGAM1708 is therefore inhibition of FLJ20511 (Accession NM\_017853). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20511. KIAA1130 (Accession XM\_031104) is another VGAM1708 host target gene. KIAA1130 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1130 BINDING SITE, designated SEQ ID:31290, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57542] Another function of VGAM1708 is therefore inhibition of KIAA1130 (Accession XM\_031104). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1130. KIAA1238 (Accession XM\_048675) is another VGAM1708 host target gene. KIAA1238 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1238, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1238 BINDING SITE, designated SEQ ID:35219, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57543] Another function of VGAM1708 is therefore inhibition of KIAA1238 (Accession XM\_048675). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1238. KIAA1466 (Accession XM\_050285) is another VGAM1708 host target gene. KIAA1466 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1466 BINDING SITE, designated SEQ ID:35604, to the nucleotide sequence of VGAM1708 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4419.

[57544] Another function of VGAM1708 is therefore inhibition of KIAA1466 (Accession XM\_050285). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1466. KIAA1536 (Accession NM\_020898) is another VGAM1708 host target gene. KIAA1536 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1536, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1536 BINDING SITE, designated SEQ ID:21926, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57545] Another function of VGAM1708 is therefore inhibition of KIAA1536 (Accession NM\_020898). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1536. KIAA1956 (Accession XM\_085836) is another VGAM1708 host target gene. KIAA1956 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1956, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1956 BINDING SITE, designated SEQ ID:38365, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57546] Another function of VGAM1708 is therefore inhibition of KIAA1956 (Accession XM\_085836). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1956. KOC1 (Accession XM\_165847) is another VGAM1708 host target gene. KOC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KOC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KOC1 BINDING SITE, designated SEQ ID:43782, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57547] Another function of VGAM1708 is therefore inhibition of KOC1 (Accession XM\_165847). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KOC1. MGC15619 (Accession NM\_032369) is another VGAM1708 host target gene. MGC15619 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15619 BINDING SITE, designated SEQ ID:26159, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57548] Another function of VGAM1708 is therefore inhibition of MGC15619 (Accession NM\_032369). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15619. MGC16824 (Accession NM\_020314) is another VGAM1708 host target gene. MGC16824 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC16824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16824 BINDING SITE, designated SEQ ID:21573, to



the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57549] Another function of VGAM1708 is therefore inhibition of MGC16824 (Accession NM\_020314). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16824. NET-2 (Accession NM\_012338) is another VGAM1708 host target gene. NET-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NET-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NET-2 BINDING SITE, designated SEQ ID:14734, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57550] Another function of VGAM1708 is therefore inhibition of NET-2 (Accession NM\_012338). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NET-2. NY-REN-60 (Accession XM\_040506) is another VGAM1708 host target gene. NY-REN-60 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of

mRNA encoded by NY-REN-60, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-60 BINDING SITE, designated SEQ ID:33320, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57551] Another function of VGAM1708 is therefore inhibition of NY-REN-60 (Accession XM\_040506). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-60. RENT2 (Accession NM\_015542) is another VGAM1708 host target gene. RENT2 BINDING SITE1 and RENT2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RENT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RENT2 BINDING SITE1 and RENT2 BINDING SITE2, designated SEQ ID:17804 and SEQ ID:27910 respectively, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57552] Another function of VGAM1708 is therefore inhibition of RENT2 (Accession NM\_015542). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RENT2. LOC146839 (Accession XM\_097107) is another VGAM1708 host target gene. LOC146839 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146839, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146839 BINDING SITE, designated SEQ ID:40757, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57553] Another function of VGAM1708 is therefore inhibition of LOC153205 (Accession XM\_098322). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153205. LOC153205 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153205, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153205 BINDING SITE, designated SEQ ID:41583, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57554] Another function of VGAM1708 is therefore inhibition of LOC153205 (Accession XM\_098322). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153205. LOC197125 (Accession XM\_113826) is another VGAM1708 host target gene. LOC197125 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197125, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197125 BINDING SITE, designated SEQ ID:42450, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57555] Another function of VGAM1708 is therefore inhibition of LOC197125 (Accession XM\_113826). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC197125. LOC56912 (Accession NM\_020153) is another VGAM1708 host target gene. LOC56912 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56912 BINDING SITE, designated SEQ ID:21366, to the nucleotide sequence of VGAM1708 RNA, herein designated VGAM RNA, also designated SEQ ID:4419.

[57556] Another function of VGAM1708 is therefore inhibition of LOC56912 (Accession NM\_020153). Accordingly, utilities of VGAM1708 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56912. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1709 (VGAM1709) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57557] VGAM1709 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1709 was detected is described hereinabove with reference to Figs. 1–8.

[57558] VGAM1709 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Semliki Forest Virus.

VGAM1709 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57559] VGAM1709 gene encodes a VGAM1709 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1709 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1709 precursor RNA is designated SEQ ID:1695, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1695 is located at position 4455 relative to the genome of Semliki Forest Virus.

[57560] VGAM1709 precursor RNA folds onto itself, forming VGAM1709 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57561] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1709 folded precursor RNA into VGAM1709 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1709 RNA is designated SEQ ID:4420, and is provided hereinbelow with reference to the sequence listing part.

[57562] VGAM1709 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1709 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1709 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57563] VGAM1709 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1709 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1709 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1709 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1709 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[57564] The complementary binding of VGAM1709 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM1709 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1709 host target RNA into VGAM1709 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57565] It is appreciated that VGAM1709 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1709 host target genes. The mRNA of each one of this plurality of VGAM1709 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1709 RNA, herein designated VGAM RNA, and which when bound by VGAM1709 RNA causes inhibition of translation of respective one or more VGAM1709 host target proteins.

[57566] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1709 gene, herein designated VGAM GENE, on one or more VGAM1709 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57567] It is yet further appreciated that a function of VGAM1709 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of viral infection by Semliki Forest Virus. Specific functions, and accordingly utilities, of VGAM1709 correlate with, and may be deduced from, the identity of the host target genes which VGAM1709 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57568] Nucleotide sequences of the VGAM1709 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1709 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1709 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1709 are further described hereinbelow with reference to Table 1.

[57569] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1709 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1709 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57570] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1709 gene, herein designated VGAM is inhibition of expression of VGAM1709 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1709 correlate with, and may be deduced from, the identity of the target genes which VGAM1709 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57571] Centromere Protein F, 350/400ka (mitosin) (CENPF, Accession NM\_016343) is a VGAM1709 host target gene. CENPF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENPF,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENPF BINDING SITE, designated SEQ ID:18469, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57572] A function of VGAM1709 is therefore inhibition of Centromere Protein F, 350/400ka (mitosin) (CENPF, Accession NM\_016343), a gene which is a protein of the nuclear matrix and regulates mitosis. Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENPF. The function of CENPF has been established by previous studies. Rattner et al. (1993) identified a human kinetochore protein with a molecular weight of approximately 400 kD. Designated centromeric protein F, it was only transiently associated with kinetochores from the onset of mitosis to metaphase. Liao et al. (1995) reported the cDNA sequence of CENPF, together with its expression and localization patterns at different stages of the HeLa cell cycle. CENPF is a protein of the nuclear matrix that gradually accumulates during the cell cycle until it reaches

peak levels in G2 and M phase cells and is rapidly degraded upon completion of mitosis. CENPF is first detected at the prekinetochore complex during late G2, and by prophase is clearly detectable as paired foci that correspond to all the centromeres. During mitosis, CENPF is associated with kinetochores from prometaphase until early anaphase and then is detected at the spindle midzone throughout the remainder of anaphase. By telophase, CENPF is concentrated within the intracellular bridge at either side of the midbody. The predicted structure of the 367-kD CENPF protein consists of two 1,600-amino acid-long coil domains that flank a central flexible core.

[57573] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57574] Liao, H.; Winkfein, R. J.; Mack, G.; Rattner, J. B.; Yen, T. J. : CENP-F is a protein of the nuclear matrix that assembles onto kinetochores at late G2 and is rapidly degraded after mitosis. *J. Cell Biol.* 130: 507-518, 1995. ; and

[57575] Liao, H.; Winkfein, R. J.; Mack, G.; Rattner, J. B.; Yen, T. J. : CENP-F is a protein of the nuclear matrix that assembles onto kinetochores at late G2 and is rapidly degraded after mitosis.

[57576] Further studies establishing the function and utilities of CENPF are found in John Hopkins OMIM database record ID 600236, and in cited publications numbered 7865–786 and 7676 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. C-type (calcium dependent, carbohydrate–recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252) is another VGAM1709 host target gene. CLECSF5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLECSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF5 BINDING SITE, designated SEQ ID:14920, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57577] Another function of VGAM1709 is therefore inhibition of C-type (calcium dependent, carbohydrate–recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF5. Carboxypeptidase

D (CPD, Accession NM\_001304) is another VGAM1709 host target gene. CPD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPD BINDING SITE, designated SEQ ID:6982, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57578] Another function of VGAM1709 is therefore inhibition of Carboxypeptidase D (CPD, Accession NM\_001304), a gene which is a membrane-bound metalloprotease. Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPD. The function of CPD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM596. Erythrocyte Membrane Protein Band 4.1 (elliptocytosis 1, RH-linked) (EPB41, Accession NM\_004437) is another VGAM1709 host target gene. EPB41 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EPB41,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41 BINDING SITE, designated SEQ ID:10722, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57579] Another function of VGAM1709 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1 (elliptocytosis 1, RH-linked) (EPB41, Accession NM\_004437), a gene which protein 4.1 is a major structural element of the erythrocyte membrane skeleton. it plays a key role in regulating membrane physical properties of mechanical stability and deformability by stabilizing spectrin-actin interaction. binds with a high affinity to glycophorin and with lower affinity to band iii protein. associates with the nuclear mitotic apparatus. Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41. The function of EPB41 has been established by previous studies. Conboy et al. (1986) reported the molecular cloning and characterization of human erythrocyte protein 4.1 cDNA and the complete amino acid sequence of the protein derived from



the nucleotide sequence. Probes prepared from the cloned erythrocyte protein 4.1 cDNA hybridized with distinct mRNA species from a wide variety of nonerythroid tissues including brain, liver, placenta, pancreas, and intestine, implying substantial homology between erythroid and nonerythroid protein 4.1. Brain protein 4.1, also known as synapsin I (OMIM Ref. No. 313440), is the best characterized of the nonerythroid forms. It is of note that brain protein 4.1 is coded by the X chromosome, whereas erythrocyte protein 4.1 is coded by chromosome 1. Conboy et al. (1986) showed by Southern blot analysis of genomic DNA from an Algerian family that in affected members the mutant protein 4.1 gene had a DNA rearrangement upstream from the initiation codon for translation. The mRNA from the mutant gene was aberrantly spliced. They assigned the gene to 1pter-p32 by hybridization of the cDNA to a panel of chromosomes separated by fluorescence-activated cell sorter. It does not necessarily follow that all Rh-linked elliptocytosis must have hemolytic anemia. The mutation can reside in the protein 4.1 gene but be of a different type which does not lead to severe hemolytic anemia. Indeed, it is known that most Rh-linked elliptocytosis is nonhemolytic. Partial deletion was found

in 1 family with elliptocytosis (Kan, 1986). Lambert et al. (1988) found an elliptocytosis family in which an apparent rearrangement of the coding region of the protein 4.1 gene led to restriction fragment length polymorphism when DNA was tested using a fragment of the cDNA that encompassed the coding region of the gene. Contrariwise, the basic defect in at least 1 form of non-Rh-linked elliptocytosis was known, namely the defect in alpha-spectrin which maps to 1q. Tang et al. (1988) compared nucleotide sequences of mRNA encoding erythroid and lymphoid protein 4.1 isoforms. The lymphoid protein 4.1 isoforms exhibited several nucleotide sequence motifs that appeared either to be inserted into or deleted from the mRNA by alternative splicing of a common mRNA precursor. One of the motifs, located within the spectrin-actin binding domain, was found only in erythroid cells and was specifically produced during erythroid cell maturation. Conboy et al. (1988) demonstrated that alternative splicing accounts for multiple isoforms of protein 4.1 in red cells. In his Figure 2, Conboy (1993) provided a map of the alternative splicing of protein 4.1 mRNA, emphasizing the total chromosome relative to many combinatorial splicing possibilities among the exons of the EPB41 gene.

There are, furthermore, 2 AUG initiation codons, 1 of which accounts for an N-terminal extension on the 80-kD gene product. By tissue screening, Baklouti et al. (1997) examined the complex pattern of alternative splicing variants of the protein 4.1 gene. They noted that many splicing variations occur in the spectrin/actin binding (SAB) domain. In particular, they found a 51-bp exon that was expressed almost exclusively in muscle. Genomic cloning revealed a total of 22 exons spanning approximately 200 kb containing the entire erythroid and nonerythroid coding sequence of the human locus. Animal model experiments lend further support to the function of EPB41. The complex EPB41 gene on human 1p encodes a diverse family of protein 4.1R isoforms. The prototypical 80-kD 4.1R in mature erythrocytes is a key component of the erythroid membrane skeleton that regulates red cell morphology and mechanical stability. To study the function of 4.1R in nucleated cells, Shi et al. (1999) generated mice with complete deficiency of all 4.1R protein isoforms. These 4.1R-null mice were viable, with moderate hemolytic anemia but no gross abnormalities. Platelet morphology and function were essentially normal. Non-erythroid 4.1R expression patterns revealed focal expres-

sion in specific neurons in the brain and in select cells of other major organs, challenging the view that 4.1R expression is widespread among nonerythroid cells.

[57580] It is appreciated that the abovementioned animal model for EPB41 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[57581] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57582] Shi, Z.-T.; Afzal, V.; Collier, B.; Patel, D.; Chasis, J. A.; Parra, M.; Lee, G.; Paszty, C.; Stevens, M.; Walensky, L.; Peters, L. L.; Mohandas, N.; Rubin, E.; Conboy, J. G. : Protein 4.1R-deficient mice are viable but have erythroid membrane skeleton abnormalities. J. Clin. Invest. 103: 331-340, 1999. ; and

[57583] Baklouti, F.; Huang, S.-C.; Vulliamy, T. J.; Delaunay, J.; Benz, E. J., Jr. : Organization of the human protein 4.1 genomic locus: new insights into the tissue-specific alternative splicing.

[57584] Further studies establishing the function and utilities of EPB41 are found in John Hopkins OMIM database record ID 130500, and in cited publications numbered 2570-2585,

2671, 12764–1276 and 12489–12514 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FUS1 (Accession NM\_007275) is another VGAM1709 host target gene. FUS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FUS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUS1 BINDING SITE, designated SEQ ID:14135, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57585] Another function of VGAM1709 is therefore inhibition of FUS1 (Accession NM\_007275), a gene which may function as a tumor suppressor. Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUS1. The function of FUS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1246. IRTA1 (Accession NM\_031282) is another VGAM1709 host target gene. IRTA1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by IRTA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRTA1 BINDING SITE, designated SEQ ID:25301, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57586] Another function of VGAM1709 is therefore inhibition of IRTA1 (Accession NM\_031282). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRTA1. Macrophage Scavenger Receptor 1 (MSR1, Accession NM\_002445) is another VGAM1709 host target gene. MSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSR1 BINDING SITE, designated SEQ ID:8285, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57587] Another function of VGAM1709 is therefore inhibition of Macrophage Scavenger Receptor 1 (MSR1, Accession

NM\_002445), a gene which plays a role in endocytosis of macromolecules. Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSR1. The function of MSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM176. Tolloid-like 1 (TLL1, Accession NM\_012464) is another VGAM1709 host target gene. TLL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TLL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLL1 BINDING SITE, designated SEQ ID:14837, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57588] Another function of VGAM1709 is therefore inhibition of Tolloid-like 1 (TLL1, Accession NM\_012464), a gene which is involved in bone morphogenesis. Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLL1. The function of TLL1 and its association with

various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1583.TOX (Accession NM\_014729) is another VGAM1709 host target gene. TOX BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOX BINDING SITE, designated SEQ ID:16324, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57589] Another function of VGAM1709 is therefore inhibition of TOX (Accession NM\_014729). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOX. TRIM (Accession NM\_016388) is another VGAM1709 host target gene. TRIM BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM BINDING SITE, designated SEQ



ID:18531, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57590] Another function of VGAM1709 is therefore inhibition of TRIM (Accession NM\_016388), a gene which plays a role in recruiting signaling proteins to the plasma membrane upon T-cell receptor (TCR) complex activation in T cells. Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM. The function of TRIM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM227. Tripartite Motif-containing 9 (TRIM9, Accession NM\_015163) is another VGAM1709 host target gene. TRIM9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRIM9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM9 BINDING SITE, designated SEQ ID:17516, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57591] Another function of VGAM1709 is therefore inhibition of Tripartite Motif-containing 9 (TRIM9, Accession NM\_015163), a gene which may function as a positive regulator for mannosylphosphate transferase and is required to mediate mannosylphosphate transfer in both the core and outer chain portions of n-linked oligosaccharides. Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM9. The function of TRIM9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.AAK1 (Accession NM\_014911) is another VGAM1709 host target gene. AAK1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AAK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AAK1 BINDING SITE, designated SEQ ID:17142, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57592] Another function of VGAM1709 is therefore inhibition of AAK1 (Accession NM\_014911). Accordingly, utilities of

VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AAK1. Acetyl-Coenzyme A Acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (ACAA2, Accession XM\_166287) is another VGAM1709 host target gene. ACAA2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ACAA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACAA2 BINDING SITE, designated SEQ ID:44094, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57593] Another function of VGAM1709 is therefore inhibition of Acetyl-Coenzyme A Acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (ACAA2, Accession XM\_166287). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACAA2. DKFZP564D166 (Accession NM\_030658) is another VGAM1709 host target gene. DKFZP564D166 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by DKFZP564D166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564D166 BINDING SITE, designated SEQ ID:24989, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57594] Another function of VGAM1709 is therefore inhibition of DKFZP564D166 (Accession NM\_030658). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D166. DKFZP564J102 (Accession XM\_038475) is another VGAM1709 host target gene. DKFZP564J102 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP564J102, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564J102 BINDING SITE, designated SEQ ID:32848, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57595] Another function of VGAM1709 is therefore inhibition of

DKFZP564J102 (Accession XM\_038475). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564J102. FLJ12488 (Accession NM\_031218) is another VGAM1709 host target gene. FLJ12488 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12488, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12488 BINDING SITE, designated SEQ ID:25263, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57596] Another function of VGAM1709 is therefore inhibition of FLJ12488 (Accession NM\_031218). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12488. FLJ13593 (Accession NM\_024780) is another VGAM1709 host target gene. FLJ13593 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13593, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ13593 BINDING SITE, designated SEQ ID:24150, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57597] Another function of VGAM1709 is therefore inhibition of FLJ13593 (Accession NM\_024780). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13593. FLJ20718 (Accession NM\_017939) is another VGAM1709 host target gene. FLJ20718 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20718, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20718 BINDING SITE, designated SEQ ID:19633, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57598] Another function of VGAM1709 is therefore inhibition of FLJ20718 (Accession NM\_017939). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20718. FLJ23511 (Accession NM\_032239) is another

VGAM1709 host target gene. FLJ23511 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ23511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23511 BINDING SITE, designated SEQ ID:25961, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57599] Another function of VGAM1709 is therefore inhibition of FLJ23511 (Accession NM\_032239). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23511. KIAA0296 (Accession NM\_014699) is another VGAM1709 host target gene. KIAA0296 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0296 BINDING SITE, designated SEQ ID:16221, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57600] Another function of VGAM1709 is therefore inhibition of KIAA0296 (Accession NM\_014699). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0296. KIAA0869 (Accession XM\_047992) is another VGAM1709 host target gene. KIAA0869 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0869, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0869 BINDING SITE, designated SEQ ID:35093, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57601] Another function of VGAM1709 is therefore inhibition of KIAA0869 (Accession XM\_047992). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0869. KIAA1054 (Accession XM\_043493) is another VGAM1709 host target gene. KIAA1054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1054, corresponding to a HOST TARGET binding site such as BINDING SITE I,



BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1054 BINDING SITE, designated SEQ ID:33955, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57602] Another function of VGAM1709 is therefore inhibition of KIAA1054 (Accession XM\_043493). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1054. MGC22014 (Accession XM\_035307) is another VGAM1709 host target gene. MGC22014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC22014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC22014 BINDING SITE, designated SEQ ID:32219, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57603] Another function of VGAM1709 is therefore inhibition of MGC22014 (Accession XM\_035307). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC22014. MGC32104 (Accession NM\_144684) is another VGAM1709 host target gene. MGC32104 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC32104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC32104 BINDING SITE, designated SEQ ID:29506, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57604] Another function of VGAM1709 is therefore inhibition of MGC32104 (Accession NM\_144684). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC32104. MGC4832 (Accession NM\_145061) is another VGAM1709 host target gene. MGC4832 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4832, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4832 BINDING SITE, designated SEQ ID:29700, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM

RNA, also designated SEQ ID:4420.

[57605] Another function of VGAM1709 is therefore inhibition of MGC4832 (Accession NM\_145061). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4832. MST4 (Accession NM\_016542) is another VGAM1709 host target gene. MST4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MST4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MST4 BINDING SITE, designated SEQ ID:18608, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57606] Another function of VGAM1709 is therefore inhibition of MST4 (Accession NM\_016542). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MST4. Pellino Homolog 2 (Drosophila) (PELI2, Accession NM\_021255) is another VGAM1709 host target gene. PELI2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PELI2,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PELI2 BINDING SITE, designated SEQ ID:22226, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57607] Another function of VGAM1709 is therefore inhibition of Pellino Homolog 2 (Drosophila) (PELI2, Accession NM\_021255). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PELI2. Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM\_014737) is another VGAM1709 host target gene. RASSF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASSF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASSF2 BINDING SITE, designated SEQ ID:16393, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57608] Another function of VGAM1709 is therefore inhibition of

Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM\_014737). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASSF2. LOC120939 (Accession XM\_073688) is another VGAM1709 host target gene. LOC120939 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC120939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120939 BINDING SITE, designated SEQ ID:37509, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57609] Another function of VGAM1709 is therefore inhibition of LOC120939 (Accession XM\_073688). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120939. LOC145978 (Accession XM\_085288) is another VGAM1709 host target gene. LOC145978 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145978, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145978 BINDING SITE, designated SEQ ID:38032, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57610] Another function of VGAM1709 is therefore inhibition of LOC145978 (Accession XM\_085288). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145978. LOC147077 (Accession XM\_085699) is another VGAM1709 host target gene. LOC147077 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147077 BINDING SITE, designated SEQ ID:38290, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57611] Another function of VGAM1709 is therefore inhibition of LOC147077 (Accession XM\_085699). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC147077. LOC154930 (Accession XM\_088080) is another VGAM1709 host target gene. LOC154930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154930 BINDING SITE, designated SEQ ID:39502, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57612] Another function of VGAM1709 is therefore inhibition of LOC154930 (Accession XM\_088080). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154930. LOC169270 (Accession XM\_095607) is another VGAM1709 host target gene. LOC169270 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169270, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169270 BINDING SITE, designated SEQ ID:40275, to the nucleotide sequence of VGAM1709 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4420.

[57613] Another function of VGAM1709 is therefore inhibition of LOC169270 (Accession XM\_095607). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169270. LOC197358 (Accession XM\_113872) is another VGAM1709 host target gene. LOC197358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197358 BINDING SITE, designated SEQ ID:42508, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57614] Another function of VGAM1709 is therefore inhibition of LOC197358 (Accession XM\_113872). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197358. LOC199775 (Accession XM\_114016) is another VGAM1709 host target gene. LOC199775 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199775, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199775 BINDING SITE, designated SEQ ID:42615, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57615] Another function of VGAM1709 is therefore inhibition of LOC199775 (Accession XM\_114016). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199775. LOC199863 (Accession XM\_117147) is another VGAM1709 host target gene. LOC199863 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199863, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199863 BINDING SITE, designated SEQ ID:43255, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57616] Another function of VGAM1709 is therefore inhibition of LOC199863 (Accession XM\_117147). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC199863. LOC219672 (Accession XM\_166111) is another VGAM1709 host target gene. LOC219672 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC219672, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219672 BINDING SITE, designated SEQ ID:43889, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57617] Another function of VGAM1709 is therefore inhibition of LOC219672 (Accession XM\_166111). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219672. LOC219894 (Accession XM\_167782) is another VGAM1709 host target gene. LOC219894 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC219894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219894 BINDING SITE, designated SEQ ID:44796, to

the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57618] Another function of VGAM1709 is therefore inhibition of LOC219894 (Accession XM\_167782). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219894. LOC220706 (Accession XM\_166001) is another VGAM1709 host target gene. LOC220706 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220706 BINDING SITE, designated SEQ ID:43837, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57619] Another function of VGAM1709 is therefore inhibition of LOC220706 (Accession XM\_166001). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220706. LOC221103 (Accession XM\_167758) is another VGAM1709 host target gene. LOC221103 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC221103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221103 BINDING SITE, designated SEQ ID:44779, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57620] Another function of VGAM1709 is therefore inhibition of LOC221103 (Accession XM\_167758). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221103. LOC222681 (Accession XM\_167116) is another VGAM1709 host target gene. LOC222681 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222681 BINDING SITE, designated SEQ ID:44616, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57621] Another function of VGAM1709 is therefore inhibition of LOC222681 (Accession XM\_167116). Accordingly, utilities

of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222681. LOC257507 (Accession XM\_175204) is another VGAM1709 host target gene. LOC257507 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257507, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257507 BINDING SITE, designated SEQ ID:46682, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57622] Another function of VGAM1709 is therefore inhibition of LOC257507 (Accession XM\_175204). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257507. LOC257625 (Accession XM\_175267) is another VGAM1709 host target gene. LOC257625 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257625, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC257625 BINDING SITE, designated SEQ ID:46738, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57623] Another function of VGAM1709 is therefore inhibition of LOC257625 (Accession XM\_175267). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257625. LOC90019 (Accession NM\_138567) is another VGAM1709 host target gene. LOC90019 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90019 BINDING SITE, designated SEQ ID:28872, to the nucleotide sequence of VGAM1709 RNA, herein designated VGAM RNA, also designated SEQ ID:4420.

[57624] Another function of VGAM1709 is therefore inhibition of LOC90019 (Accession NM\_138567). Accordingly, utilities of VGAM1709 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90019. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1710 (VGAM1710) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57625] VGAM1710 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1710 was detected is described hereinabove with reference to Figs. 1–8.

[57626] VGAM1710 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Semliki Forest Virus. VGAM1710 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57627] VGAM1710 gene encodes a VGAM1710 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1710 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1710 precursor RNA is designated SEQ ID:1696, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1696 is located at position 7249 relative to the

genome of Semliki Forest Virus.

[57628] VGAM1710 precursor RNA folds onto itself, forming VGAM1710 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57629] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1710 folded precursor RNA into VGAM1710 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1710 RNA is designated SEQ ID:4421, and is provided hereinbelow with reference to the sequence listing part.

[57630] VGAM1710 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1710 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1710 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[57631] VGAM1710 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1710 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1710 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1710 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1710 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57632] The complementary binding of VGAM1710 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1710 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1710 host target RNA into VGAM1710 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57633] It is appreciated that VGAM1710 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1710 host target genes. The mRNA of each one of this plurality of VGAM1710 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1710 RNA, herein designated VGAM RNA, and which when bound by VGAM1710 RNA causes inhibition of translation of respective one or more VGAM1710 host target proteins.

[57634] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1710 gene, herein designated VGAM GENE, on one or more VGAM1710 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57635] It is yet further appreciated that a function of VGAM1710 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of viral infection by Semliki Forest Virus. Specific functions, and accordingly utilities, of VGAM1710

correlate with, and may be deduced from, the identity of the host target genes which VGAM1710 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57636] Nucleotide sequences of the VGAM1710 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1710 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1710 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1710 are further described hereinbelow with reference to Table 1.

[57637] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1710 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1710 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57638] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1710 gene, herein designated VGAM is inhibition of expression of VGAM1710 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1710 correlate with, and may be deduced

from, the identity of the target genes which VGAM1710 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57639] Cytokine Inducible SH2-containing Protein (CISH, Accession NM\_013324) is a VGAM1710 host target gene. CISH BINDING SITE1 and CISH BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CISH, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CISH BINDING SITE1 and CISH BINDING SITE2, designated SEQ ID:14973 and SEQ ID:29706 respectively, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57640] A function of VGAM1710 is therefore inhibition of Cytokine Inducible SH2-containing Protein (CISH, Accession NM\_013324), a gene which intervenes in the negative regulation of cytokines. Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CISH. The function of CISH and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM488.Chromosome 20 Open Reading Frame 162 (C20orf162, Accession NM\_080603) is another VGAM1710 host target gene. C20orf162 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C20orf162, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf162 BINDING SITE, designated SEQ ID:27919, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57641] Another function of VGAM1710 is therefore inhibition of Chromosome 20 Open Reading Frame 162 (C20orf162, Accession NM\_080603). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf162. FLJ20297 (Accession NM\_017951) is another VGAM1710 host target gene. FLJ20297 BINDING SITE1 and FLJ20297 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ20297, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20297 BINDING SITE1 and FLJ20297 BINDING SITE2, designated SEQ ID:19653 and SEQ ID:19361 respectively, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57642] Another function of VGAM1710 is therefore inhibition of FLJ20297 (Accession NM\_017951). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20297. ZER6 (Accession XM\_032742) is another VGAM1710 host target gene. ZER6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZER6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZER6 BINDING SITE, designated SEQ ID:31744, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57643] Another function of VGAM1710 is therefore inhibition of ZER6 (Accession XM\_032742). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ZER6. LOC126661 (Accession XM\_059061) is another VGAM1710 host target gene. LOC126661 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC126661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126661 BINDING SITE, designated SEQ ID:36848, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57644] Another function of VGAM1710 is therefore inhibition of LOC126661 (Accession XM\_059061). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126661. LOC144467 (Accession NM\_138473) is another VGAM1710 host target gene. LOC144467 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144467, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144467 BINDING SITE, designated SEQ ID:28821, to



the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57645] Another function of VGAM1710 is therefore inhibition of LOC144467 (Accession NM\_138473). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144467. LOC149830 (Accession XM\_097746) is another VGAM1710 host target gene. LOC149830 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149830, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149830 BINDING SITE, designated SEQ ID:41095, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57646] Another function of VGAM1710 is therefore inhibition of LOC149830 (Accession XM\_097746). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149830. LOC150776 (Accession XM\_032542) is another VGAM1710 host target gene. LOC150776 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC150776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150776 BINDING SITE, designated SEQ ID:31679, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57647] Another function of VGAM1710 is therefore inhibition of LOC150776 (Accession XM\_032542). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150776. LOC152359 (Accession XM\_098213) is another VGAM1710 host target gene. LOC152359 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152359, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152359 BINDING SITE, designated SEQ ID:41491, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57648] Another function of VGAM1710 is therefore inhibition of LOC152359 (Accession XM\_098213). Accordingly, utilities

of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152359. LOC154930 (Accession XM\_088080) is another VGAM1710 host target gene. LOC154930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154930 BINDING SITE, designated SEQ ID:39506, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57649] Another function of VGAM1710 is therefore inhibition of LOC154930 (Accession XM\_088080). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154930. LOC221103 (Accession XM\_167758) is another VGAM1710 host target gene. LOC221103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC221103 BINDING SITE, designated SEQ ID:44778, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57650] Another function of VGAM1710 is therefore inhibition of LOC221103 (Accession XM\_167758). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221103. LOC253120 (Accession XM\_172575) is another VGAM1710 host target gene. LOC253120 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253120 BINDING SITE, designated SEQ ID:46076, to the nucleotide sequence of VGAM1710 RNA, herein designated VGAM RNA, also designated SEQ ID:4421.

[57651] Another function of VGAM1710 is therefore inhibition of LOC253120 (Accession XM\_172575). Accordingly, utilities of VGAM1710 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253120. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1711 (VGAM1711) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57652] VGAM1711 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1711 was detected is described hereinabove with reference to Figs. 1–8.

[57653] VGAM1711 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Semliki Forest Virus. VGAM1711 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57654] VGAM1711 gene encodes a VGAM1711 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1711 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1711 precursor RNA is designated SEQ ID:1697, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1697 is located at position 4081 relative to the

genome of Semliki Forest Virus.

[57655] VGAM1711 precursor RNA folds onto itself, forming VGAM1711 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57656] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1711 folded precursor RNA into VGAM1711 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1711 RNA is designated SEQ ID:4422, and is provided hereinbelow with reference to the sequence listing part.

[57657] VGAM1711 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1711 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1711 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57658] VGAM1711 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1711 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1711 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1711 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1711 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[57659] The complementary binding of VGAM1711 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1711 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1711 host target RNA into VGAM1711 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57660] It is appreciated that VGAM1711 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1711 host target genes. The mRNA of each one of this plurality of VGAM1711 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1711 RNA, herein designated VGAM RNA, and which when bound by VGAM1711 RNA causes inhibition of translation of respective one or more VGAM1711 host target proteins.



[57661] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1711 gene, herein designated VGAM GENE, on one or more VGAM1711 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57662] It is yet further appreciated that a function of VGAM1711 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of viral infection by Semliki Forest Virus. Specific functions, and accordingly utilities, of VGAM1711

correlate with, and may be deduced from, the identity of the host target genes which VGAM1711 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57663] Nucleotide sequences of the VGAM1711 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1711 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1711 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1711 are further described hereinbelow with reference to Table 1.

[57664] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1711 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1711 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57665] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1711 gene, herein designated VGAM is inhibition of expression of VGAM1711 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1711 correlate with, and may be deduced

from, the identity of the target genes which VGAM1711 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57666] Adenylate Cyclase 2 (brain) (ADCY2, Accession XM\_036383) is a VGAM1711 host target gene. ADCY2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADCY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY2 BINDING SITE, designated SEQ ID:32434, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57667] A function of VGAM1711 is therefore inhibition of Adenylate Cyclase 2 (brain) (ADCY2, Accession XM\_036383), a gene which Adenylate cyclase (type 2), an ATP-pyrophosphate lyase; converts ATP to cAMP. Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY2. The function of ADCY2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Apolipoprotein L, 1 (APOL1,

Accession NM\_003661) is another VGAM1711 host target gene. APOL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL1 BINDING SITE, designated SEQ ID:9733, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57668] Another function of VGAM1711 is therefore inhibition of Apolipoprotein L, 1 (APOL1, Accession NM\_003661), a gene which may participate in reverse cholesterol transport from peripheral cells to the liver. Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL1. The function of APOL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM235. Activating Transcription Factor 5 (ATF5, Accession NM\_012068) is another VGAM1711 host target gene. ATF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by ATF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATF5 BINDING SITE, designated SEQ ID:14321, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57669] Another function of VGAM1711 is therefore inhibition of Activating Transcription Factor 5 (ATF5, Accession NM\_012068), a gene which binds to cAMP-inducible promoters and is involved in gene transcription. Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATF5. The function of ATF5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM588. Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 5 (CHST5, Accession NM\_012126) is another VGAM1711 host target gene. CHST5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHST5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of CHST5 BINDING SITE, designated SEQ ID:14440, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57670] Another function of VGAM1711 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 5 (CHST5, Accession NM\_012126), a gene which may be involved in sulfation of glycoproteins and proteoglycans. Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST5. The function of CHST5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM186. Cryptochrome 2 (photolyase-like) (CRY2, Accession XM\_051030) is another VGAM1711 host target gene. CRY2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRY2 BINDING SITE, designated SEQ ID:35732,

to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57671] Another function of VGAM1711 is therefore inhibition of Cryptochrome 2 (photolyase-like) (CRY2, Accession XM\_051030), a gene which has a role in circadian photoreception in mammals. Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRY2. The function of CRY2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1223. EGF-like-domain, Multiple 5 (EGFL5, Accession XM\_098838) is another VGAM1711 host target gene. EGFL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL5 BINDING SITE, designated SEQ ID:41883, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57672] Another function of VGAM1711 is therefore inhibition of

EGF-like-domain, Multiple 5 (EGFL5, Accession XM\_098838). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL5. Glutamine-fructose-6-phosphate Transaminase 2 (GFPT2, Accession NM\_005110) is another VGAM1711 host target gene. GFPT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFPT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFPT2 BINDING SITE, designated SEQ ID:11593, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57673] Another function of VGAM1711 is therefore inhibition of Glutamine-fructose-6-phosphate Transaminase 2 (GFPT2, Accession NM\_005110). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFPT2. Glucagon-like Peptide 1 Receptor (GLP1R, Accession NM\_002062) is another VGAM1711 host target gene. GLP1R BINDING SITE is HOST TARGET binding site found



in the 3` untranslated region of mRNA encoded by GLP1R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLP1R BINDING SITE, designated SEQ ID:7826, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57674] Another function of VGAM1711 is therefore inhibition of Glucagon-like Peptide 1 Receptor (GLP1R, Accession NM\_002062), a gene which is mediated by g proteins which activate adenylyl cyclase. Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLP1R. The function of GLP1R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1652. Interleukin-1 Receptor-associated Kinase 1 (IRAK1, Accession NM\_001569) is another VGAM1711 host target gene. IRAK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IRAK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of IRAK1 BINDING SITE, designated SEQ ID:7300, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57675] Another function of VGAM1711 is therefore inhibition of Interleukin-1 Receptor-associated Kinase 1 (IRAK1, Accession NM\_001569). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRAK1. Kinesin Family Member 3B (KIF3B, Accession NM\_004798) is another VGAM1711 host target gene. KIF3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF3B BINDING SITE, designated SEQ ID:11217, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57676] Another function of VGAM1711 is therefore inhibition of Kinesin Family Member 3B (KIF3B, Accession NM\_004798), a gene which is a microtubule-based anterograde translocator for membranous organelles. Accordingly, utilities of

VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF3B. The function of KIF3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1017. Leptin (obesity homolog, mouse) (LEP, Accession NM\_000230) is another VGAM1711 host target gene. LEP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEP BINDING SITE, designated SEQ ID:5740, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57677] Another function of VGAM1711 is therefore inhibition of Leptin (obesity homolog, mouse) (LEP, Accession NM\_000230). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEP. LIM Homeobox Protein 1 (LHX1, Accession NM\_005568) is another VGAM1711 host target gene. LHX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by LHX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LHX1 BINDING SITE, designated SEQ ID:12093, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57678] Another function of VGAM1711 is therefore inhibition of LIM Homeobox Protein 1 (LHX1, Accession NM\_005568). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LHX1. LIM Domain Only 2 (rhombotin-like 1) (LMO2, Accession NM\_005574) is another VGAM1711 host target gene. LMO2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LMO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMO2 BINDING SITE, designated SEQ ID:12102, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57679] Another function of VGAM1711 is therefore inhibition of

LIM Domain Only 2 (rhombotin-like 1) (LMO2, Accession NM\_005574). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMO2. Myelin Oligodendrocyte Glycoprotein (MOG, Accession NM\_002433) is another VGAM1711 host target gene. MOG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MOG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOG BINDING SITE, designated SEQ ID:8279, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57680] Another function of VGAM1711 is therefore inhibition of Myelin Oligodendrocyte Glycoprotein (MOG, Accession NM\_002433). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOG. Paired-like Homeodomain Transcription Factor 3 (PITX3, Accession NM\_005029) is another VGAM1711 host target gene. PITX3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PITX3,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PITX3 BINDING SITE, designated SEQ ID:11470, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57681] Another function of VGAM1711 is therefore inhibition of Paired-like Homeodomain Transcription Factor 3 (PITX3, Accession NM\_005029), a gene which may play a role in normal anterior-chamber and lens development. Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PITX3. The function of PITX3 has been established by previous studies. The PITX3 gene is the human homolog of the mouse Pitx3 gene and is a member of the RIEG/PITX homeo box gene family. The protein encoded by PITX3 shows 99% amino acid identity to the mouse Pitx3 protein, with 100% identity in the homeodomain and approximately 70% overall identity to other members of this family. Semina et al. (1998) screened a collection of 80 DNA samples from individuals with various eye anomalies for mutations in the PITX3 gene. A mutation was identified in each of 2 unrelated patients. The 17-bp

insertion in the 3-prime end of the coding sequence, resulting in a frameshift (602669.0001), occurred in a patient with anterior segment mesenchymal dysgenesis (ASMD; 107250) and cataracts; a G-to-A substitution in the 5-prime end of the gene, changing a codon for serine into a codon for asparagine (602669.0002), occurred in a patient with congenital cataracts. Each mutation cosegregated with the disease phenotype in families and was not found in up to 300 control individuals studied. Further expression analysis of Pitx3 in the mouse supported a unique role in early ocular development, with later expression extending to the midbrain, tongue, incisors, sternum, vertebrae, and limbs. The findings strongly suggested the role of PITX3 in ASMD and cataracts and provided new evidence of the contribution of the RIEG/PITX gene family to the developmental program underpinning normal eye formation. The PTX1 (OMIM Ref. No. 601542), PTX2 (OMIM Ref. No. 602149), and PTX3 genes define a novel family of transcription factors, the PTX subfamily, within the paired-like class of homeodomain factors. In mice, Ptx1 and Ptx2 gene expression has been detected in the area of the pituitary primordium and is maintained throughout development in the Rathke pouch and adult

pituitary. Pellegrini-Bouiller et al. (1999) characterized the expression of the PTX1, PTX2, and PTX3 genes in the normal human pituitary and in the different types of human pituitary adenomas. RT-PCR analysis detected no PTX3 expression in adult and fetal normal human pituitary, although a specific band was readily amplified from fetal mesencephalon, a tissue known to express this gene. Animal model experiments lend further support to the function of PITX3. Mouse 'aphakia' (ak) is a recessive phenotype that spontaneously occurs in the 129/Sv-SIJ strain and is characterized by small eyes that lack a lens. Semina et al. (1997) determined that the Pitx3 gene is expressed in the developing lens and maps to chromosome 19, close to ak in mouse. In further studies, Semina et al. (2000) did not detect by in situ hybridization Pitx3 transcripts in ak/ak mice, either in the lens placode or at later developmental stages of the lens. Although no differences were previously found between ak/ak and wildtype sequences in the Pitx3 coding region, the authors identified a deletion of 652 bp located 2.5 kb upstream from the start point of the Pitx3 5-prime untranslated region sequence in ak/ak mice. The deletion cosegregated with the ak mutation and was not detected in 16 samples from 10 differ-



ent mouse strains, including the founder strains. Analysis of the 652-bp region identified sequences similar to consensus binding sites for transcription factors AP2 (see OMIM Ref. No. 107580) and Maf (see OMIM Ref. No. 177075) that were shown to play a critical role in lens determination. The authors concluded that the abnormal ocular development in the aphakia mouse is due to the deletion upstream of the Pitx3 gene.

[57682] It is appreciated that the abovementioned animal model for PITX3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[57683] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57684] Semina, E. V.; Ferrell, R. E.; Mintz-Hittner, H. A.; Bitoun, P.; Alward, W. L. M.; Reiter, R. S.; Funkhauser, C.; Daack-Hirsch, S.; Murray, J. C. : A novel homeobox gene PITX3 is mutated in families with autosomal-dominant cataracts and ASMD. *Nature Genet.* 19: 167-170, 1998. ; and

[57685] Semina, E. V.; Murray, J. C.; Reiter, R.; Hrstka, R. F.; Graw, J. : Deletion in the promoter region and altered expression of Pitx3 homeobox gene in aphakia mice. *Hum. Molec.*

Genet. 9:.

[57686] Further studies establishing the function and utilities of PITX3 are found in John Hopkins OMIM database record ID 602669, and in cited publications numbered 876 and 8944–8764 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Suppression of Tumorigenicity 5 (ST5, Accession NM\_005418) is another VGAM1711 host target gene. ST5 BINDING SITE1 and ST5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ST5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST5 BINDING SITE1 and ST5 BINDING SITE2, designated SEQ ID:11889 and SEQ ID:29169 respectively, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57687] Another function of VGAM1711 is therefore inhibition of Suppression of Tumorigenicity 5 (ST5, Accession NM\_005418), a gene which preferentially binds to the SH3 domain of c-Abl kinase, and acts as a regulator of MAPK1/ERK2 kinase. Accordingly, utilities of VGAM1711

include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST5. The function of ST5 has been established by previous studies. The tumorigenicity of HeLa cells in nude mice can be suppressed by the addition of a normal human chromosome 11 in somatic cell hybrids (Stanbridge, 1976; Klinger, 1980); see 191181 for description of a tumor-suppressor gene located on 11q. Lichy et al. (1992) isolated a HeLa cell line that displayed morphologic features of the nontumorigenic hybrids, demonstrated reduced tumorigenicity in nude mice, and showed an 85% reduction in alkaline phosphatase, a consistent marker of the tumorigenic phenotype in these cells. This cell line, designated F2, contained a single exogenous cDNA, which was recovered by polymerase chain reaction (PCR) and designated HTS1 because of its probable association with 'HeLa tumor suppression.' In nontumorigenic hybrids, RNA species of 2.8, 3.1, and 4.6 kb were identified. In 2 tumorigenic hybrid lines, the 2.8-kb species was markedly reduced or absent. Whereas 3 nontumorigenic human keratinocyte lines expressed all 3 RNA species, several tumorigenic cervical carcinoma cell lines lacked the 2.8-kb species. The HTS1 gene was localized to 11p15 by in situ hybridization, con-

firming the assignment to chromosome 11 by somatic cell hybrid analysis. Lichy et al. (1992) reviewed previous evidence indicating the presence of a tumor suppressor gene in the 11p15 region; see 194071 and 185440.

[57688] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57689] Lichy, J. H.; Modi, W. S.; Seuanez, H. N.; Howley, P. M. : Identification of a human chromosome 11 gene which is differentially regulated in tumorigenic and nontumorigenic somatic cell hybrids of HeLa cells. *Cell Growth Differ.* 3: 541–548, 1992. ; and

[57690] Stanbridge, E. J. : Suppression of malignancy in human cells. *Nature* 260: 17–20, 1976.

[57691] Further studies establishing the function and utilities of ST5 are found in John Hopkins OMIM database record ID 140750, and in cited publications numbered 12003–12005 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. 1-acylglycerol-3-phosphate O-acyltransferase 1 (lysophosphatidic acid acyltransferase, alpha) (AGPAT1, Accession NM\_032741) is another VGAM1711 host target gene. AGPAT1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by AGPAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGPAT1 BINDING SITE, designated SEQ ID:26473, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57692] Another function of VGAM1711 is therefore inhibition of 1-acylglycerol-3-phosphate O-acyltransferase 1 (lysophosphatidic acid acyltransferase, alpha) (AGPAT1, Accession NM\_032741). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGPAT1. Aldo-keto Reductase Family 1, Member D1 (delta 4-3-ketosteroid-5-beta-reductase) (AKR1D1, Accession NM\_005989) is another VGAM1711 host target gene. AKR1D1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKR1D1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKR1D1 BINDING SITE, designated SEQ

ID:12611, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57693] Another function of VGAM1711 is therefore inhibition of Aldo-keto Reductase Family 1, Member D1 (delta 4-3-ketosteroid-5-beta-reductase) (AKR1D1, Accession NM\_005989). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKR1D1. Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM\_018270) is another VGAM1711 host target gene. C20orf20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf20 BINDING SITE, designated SEQ ID:20245, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57694] Another function of VGAM1711 is therefore inhibition of Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM\_018270). Accordingly, utilities of VGAM1711

include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf20.

FLJ10547 (Accession NM\_018134) is another VGAM1711 host target gene. FLJ10547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10547 BINDING SITE, designated SEQ ID:19931, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57695] Another function of VGAM1711 is therefore inhibition of FLJ10547 (Accession NM\_018134). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10547. FLJ11577 (Accession NM\_025159) is another VGAM1711 host target gene. FLJ11577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11577

BINDING SITE, designated SEQ ID:24800, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57696] Another function of VGAM1711 is therefore inhibition of FLJ11577 (Accession NM\_025159). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11577. FLJ20079 (Accession NM\_017656) is another VGAM1711 host target gene. FLJ20079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19174, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57697] Another function of VGAM1711 is therefore inhibition of FLJ20079 (Accession NM\_017656). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. FLJ20306 (Accession NM\_017756) is another VGAM1711 host target gene. FLJ20306 BINDING SITE is



HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20306 BINDING SITE, designated SEQ ID:19369, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57698] Another function of VGAM1711 is therefore inhibition of FLJ20306 (Accession NM\_017756). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20306. FLJ22167 (Accession NM\_024533) is another VGAM1711 host target gene. FLJ22167 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22167, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22167 BINDING SITE, designated SEQ ID:23742, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57699] Another function of VGAM1711 is therefore inhibition of

FLJ22167 (Accession NM\_024533). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22167. FLJ22615 (Accession XM\_043654) is another VGAM1711 host target gene. FLJ22615 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22615, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22615 BINDING SITE, designated SEQ ID:33991, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57700] Another function of VGAM1711 is therefore inhibition of FLJ22615 (Accession XM\_043654). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22615. FLJ22635 (Accession NM\_025092) is another VGAM1711 host target gene. FLJ22635 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ22635 BINDING SITE, designated SEQ ID:24717, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57701] Another function of VGAM1711 is therefore inhibition of FLJ22635 (Accession NM\_025092). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22635. FLJ22814 (Accession NM\_024916) is another VGAM1711 host target gene. FLJ22814 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22814, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22814 BINDING SITE, designated SEQ ID:24442, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57702] Another function of VGAM1711 is therefore inhibition of FLJ22814 (Accession NM\_024916). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22814. Glycoprotein A33 (transmembrane) (GPA33, Ac-

cession NM\_005814) is another VGAM1711 host target gene. GPA33 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPA33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPA33 BINDING SITE, designated SEQ ID:12404, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57703] Another function of VGAM1711 is therefore inhibition of Glycoprotein A33 (transmembrane) (GPA33, Accession NM\_005814). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPA33. HSRNAFEV (Accession NM\_017521) is another VGAM1711 host target gene. HSRNAFEV BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSRNAFEV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSRNAFEV BINDING SITE, designated SEQ ID:18969, to the nucleotide sequence of

VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57704] Another function of VGAM1711 is therefore inhibition of HSRNAFEV (Accession NM\_017521). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSRNAFEV. KIAA0057 (Accession NM\_012288) is another VGAM1711 host target gene. KIAA0057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0057 BINDING SITE, designated SEQ ID:14621, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57705] Another function of VGAM1711 is therefore inhibition of KIAA0057 (Accession NM\_012288). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0057. KIAA0284 (Accession XM\_032235) is another VGAM1711 host target gene. KIAA0284 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0284, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0284 BINDING SITE, designated SEQ ID:31618, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57706] Another function of VGAM1711 is therefore inhibition of KIAA0284 (Accession XM\_032235). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0284. KIAA0710 (Accession NM\_014871) is another VGAM1711 host target gene. KIAA0710 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0710, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0710 BINDING SITE, designated SEQ ID:16992, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57707] Another function of VGAM1711 is therefore inhibition of KIAA0710 (Accession NM\_014871). Accordingly, utilities

of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0710. KIAA0716 (Accession NM\_014705) is another VGAM1711 host target gene. KIAA0716 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0716, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0716 BINDING SITE, designated SEQ ID:16247, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57708] Another function of VGAM1711 is therefore inhibition of KIAA0716 (Accession NM\_014705). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0716. KIAA1228 (Accession XM\_036408) is another VGAM1711 host target gene. KIAA1228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1228 BINDING SITE, designated SEQ ID:32446, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57709] Another function of VGAM1711 is therefore inhibition of KIAA1228 (Accession XM\_036408). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1228. KIAA1969 (Accession XM\_086098) is another VGAM1711 host target gene. KIAA1969 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1969, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1969 BINDING SITE, designated SEQ ID:38492, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57710] Another function of VGAM1711 is therefore inhibition of KIAA1969 (Accession XM\_086098). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1969. MGC2452 (Accession NM\_032644) is another VGAM1711 host target gene. MGC2452 BINDING SITE is



HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2452 BINDING SITE, designated SEQ ID:26371, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57711] Another function of VGAM1711 is therefore inhibition of MGC2452 (Accession NM\_032644). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2452. Mitochondrial Ribosomal Protein 63 (MRP63, Accession NM\_024026) is another VGAM1711 host target gene. MRP63 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRP63, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRP63 BINDING SITE, designated SEQ ID:23456, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57712] Another function of VGAM1711 is therefore inhibition of Mitochondrial Ribosomal Protein 63 (MRP63, Accession NM\_024026). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRP63. Mitochondrial Ribosomal Protein L20 (MRPL20, Accession NM\_017971) is another VGAM1711 host target gene. MRPL20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL20 BINDING SITE, designated SEQ ID:19697, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57713] Another function of VGAM1711 is therefore inhibition of Mitochondrial Ribosomal Protein L20 (MRPL20, Accession NM\_017971). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL20. Neuronal Guanine Nucleotide Exchange Factor (NGEF, Accession XM\_044799) is another VGAM1711 host target gene. NGEF BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by NGEF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGEF BINDING SITE, designated SEQ ID:34277, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57714] Another function of VGAM1711 is therefore inhibition of Neuronal Guanine Nucleotide Exchange Factor (NGEF, Accession XM\_044799). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGEF. PRO0529 (Accession NM\_014074) is another VGAM1711 host target gene. PRO0529 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0529 BINDING SITE, designated SEQ ID:15299, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57715] Another function of VGAM1711 is therefore inhibition of

PRO0529 (Accession NM\_014074). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0529. Protein Tyrosine Phosphatase, Receptor Type, U (PTPRU, Accession NM\_133177) is another VGAM1711 host target gene. PTPRU BINDING SITE1 through PTPRU BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRU, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRU BINDING SITE1 through PTPRU BINDING SITE3, designated SEQ ID:28401, SEQ ID:28406 and SEQ ID:12256 respectively, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[577<sup>16</sup>] Another function of VGAM1711 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, U (PTPRU, Accession NM\_133177). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRU. Polymerase I and Transcript Release Factor (PTRF, Accession XM\_032852) is another VGAM1711 host target gene.

PTRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTRF BINDING SITE, designated SEQ ID:31783, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57717] Another function of VGAM1711 is therefore inhibition of Polymerase I and Transcript Release Factor (PTRF, Accession XM\_032852). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTRF. Smith-Magenis Syndrome Chromosome Region, Candidate 5 (SMCR5, Accession NM\_144774) is another VGAM1711 host target gene. SMCR5 BINDING SITE1 and SMCR5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMCR5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMCR5 BINDING SITE1 and SMCR5 BINDING SITE2, designated SEQ ID:29563 and SEQ ID:29564 respectively, to the nu-

cleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57718] Another function of VGAM1711 is therefore inhibition of Smith–Magenis Syndrome Chromosome Region, Candidate 5 (SMCR5, Accession NM\_144774). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMCR5. UBCE7IP5 (Accession NM\_014948) is another VGAM1711 host target gene. UBCE7IP5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by UBCE7IP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBCE7IP5 BINDING SITE, designated SEQ ID:17272, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57719] Another function of VGAM1711 is therefore inhibition of UBCE7IP5 (Accession NM\_014948). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBCE7IP5. Zinc Finger Protein 212 (ZNF212, Accession NM\_012256) is another VGAM1711 host target gene.

ZNF212 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF212, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF212 BINDING SITE, designated SEQ ID:14558, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57720] Another function of VGAM1711 is therefore inhibition of Zinc Finger Protein 212 (ZNF212, Accession NM\_012256). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF212. LOC134147 (Accession NM\_138809) is another VGAM1711 host target gene. LOC134147 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC134147, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134147 BINDING SITE, designated SEQ ID:29032, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4422.

[57721] Another function of VGAM1711 is therefore inhibition of LOC134147 (Accession NM\_138809). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134147. LOC138307 (Accession XM\_059963) is another VGAM1711 host target gene. LOC138307 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC138307, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138307 BINDING SITE, designated SEQ ID:37123, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57722] Another function of VGAM1711 is therefore inhibition of LOC138307 (Accession XM\_059963). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138307. LOC145195 (Accession XM\_096731) is another VGAM1711 host target gene. LOC145195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145195, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145195 BINDING SITE, designated SEQ ID:40513, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57723] Another function of VGAM1711 is therefore inhibition of LOC145195 (Accession XM\_096731). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145195. LOC146780 (Accession XM\_097086) is another VGAM1711 host target gene. LOC146780 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146780, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146780 BINDING SITE, designated SEQ ID:40743, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57724] Another function of VGAM1711 is therefore inhibition of LOC146780 (Accession XM\_097086). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC146780. LOC150935 (Accession XM\_087049) is another VGAM1711 host target gene. LOC150935 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC150935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150935 BINDING SITE, designated SEQ ID:39020, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57725] Another function of VGAM1711 is therefore inhibition of LOC150935 (Accession XM\_087049). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150935. LOC152804 (Accession XM\_098266) is another VGAM1711 host target gene. LOC152804 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152804, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152804 BINDING SITE, designated SEQ ID:41556, to

the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57726] Another function of VGAM1711 is therefore inhibition of LOC152804 (Accession XM\_098266). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152804. LOC162137 (Accession XM\_102426) is another VGAM1711 host target gene. LOC162137 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC162137, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162137 BINDING SITE, designated SEQ ID:42115, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57727] Another function of VGAM1711 is therefore inhibition of LOC162137 (Accession XM\_102426). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162137. LOC166867 (Accession XM\_094142) is another VGAM1711 host target gene. LOC166867 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC166867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166867 BINDING SITE, designated SEQ ID:40223, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57728] Another function of VGAM1711 is therefore inhibition of LOC166867 (Accession XM\_094142). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166867. LOC197201 (Accession XM\_113839) is another VGAM1711 host target gene. LOC197201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197201 BINDING SITE, designated SEQ ID:42464, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57729] Another function of VGAM1711 is therefore inhibition of LOC197201 (Accession XM\_113839). Accordingly, utilities

of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197201. LOC199957 (Accession XM\_114068) is another VGAM1711 host target gene. LOC199957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199957 BINDING SITE, designated SEQ ID:42675, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57730] Another function of VGAM1711 is therefore inhibition of LOC199957 (Accession XM\_114068). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199957. LOC202052 (Accession XM\_117355) is another VGAM1711 host target gene. LOC202052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC202052 BINDING SITE, designated SEQ ID:43408, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57731] Another function of VGAM1711 is therefore inhibition of LOC202052 (Accession XM\_117355). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202052. LOC203042 (Accession XM\_117490) is another VGAM1711 host target gene. LOC203042 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203042 BINDING SITE, designated SEQ ID:43475, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57732] Another function of VGAM1711 is therefore inhibition of LOC203042 (Accession XM\_117490). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203042. LOC219722 (Accession XM\_167593) is another VGAM1711 host target gene. LOC219722 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC219722, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219722 BINDING SITE, designated SEQ ID:44709, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57733] Another function of VGAM1711 is therefore inhibition of LOC219722 (Accession XM\_167593). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219722. LOC221271 (Accession XM\_166307) is another VGAM1711 host target gene. LOC221271 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221271 BINDING SITE, designated SEQ ID:44125, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57734] Another function of VGAM1711 is therefore inhibition of

LOC221271 (Accession XM\_166307). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221271. LOC221410 (Accession XM\_166373) is another VGAM1711 host target gene. LOC221410 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221410, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221410 BINDING SITE, designated SEQ ID:44195, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57735] Another function of VGAM1711 is therefore inhibition of LOC221410 (Accession XM\_166373). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221410. LOC90509 (Accession XM\_032209) is another VGAM1711 host target gene. LOC90509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-



trates the complementarity of the nucleotide sequences of LOC90509 BINDING SITE, designated SEQ ID:31608, to the nucleotide sequence of VGAM1711 RNA, herein designated VGAM RNA, also designated SEQ ID:4422.

[57736] Another function of VGAM1711 is therefore inhibition of LOC90509 (Accession XM\_032209). Accordingly, utilities of VGAM1711 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90509. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1712 (VGAM1712) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57737] VGAM1712 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1712 was detected is described hereinabove with reference to Figs. 1–8.

[57738] VGAM1712 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sindbis Virus.

VGAM1712 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[57739] VGAM1712 gene encodes a VGAM1712 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1712 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1712 precursor RNA is designated SEQ ID:1698, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1698 is located at position 8817 relative to the genome of Sindbis Virus.

[57740] VGAM1712 precursor RNA folds onto itself, forming VGAM1712 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57741] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1712 folded precursor RNA into VGAM1712 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1712 RNA is designated SEQ ID:4423, and is provided hereinbelow with reference to the sequence listing part.

[57742] VGAM1712 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1712 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1712 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57743] VGAM1712 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1712 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1712 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1712 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1712 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57744] The complementary binding of VGAM1712 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1712 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1712 host target RNA into VGAM1712 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57745] It is appreciated that VGAM1712 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1712 host target genes. The mRNA of each one of this plurality of VGAM1712 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1712 RNA, herein designated VGAM RNA, and which when bound by VGAM1712 RNA causes inhibition of translation of respective one or more VGAM1712 host target proteins.

[57746] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1712 gene, herein designated VGAM GENE, on one or more VGAM1712 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57747] It is yet further appreciated that a function of VGAM1712 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1712 include diagnosis, prevention and treatment of viral infection by Sindbis Virus. Specific functions, and accordingly utilities, of VGAM1712 correlate with, and may be deduced from, the identity of the host target genes which VGAM1712 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57748] Nucleotide sequences of the VGAM1712 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1712 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1712 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1712 are further described hereinbelow with reference to Table 1.

[57749] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1712 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1712 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57750] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1712 gene, herein designated VGAM is inhibition of expression of VGAM1712 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1712 correlate with, and may be deduced from, the identity of the target genes which VGAM1712 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57751] EphB3 (EPHB3, Accession NM\_004443) is a VGAM1712 host target gene. EPHB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHB3 BINDING SITE, designated SEQ ID:10736, to the nucleotide sequence of VGAM1712 RNA, herein designated VGAM RNA, also designated SEQ ID:4423.

[57752] A function of VGAM1712 is therefore inhibition of EphB3 (EPHB3, Accession NM\_004443), a gene which receptor for members of the ephrin-b family. binds to ephrin-b1 and -b2. Accordingly, utilities of VGAM1712 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHB3. The function of EPHB3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM455. Heat Shock 70kDa Protein 9B (mortalin-2) (HSPA9B, Accession NM\_004134) is another VGAM1712 host target gene. HSPA9B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPA9B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPA9B BINDING SITE, designated SEQ ID:10347, to the nucleotide sequence of VGAM1712 RNA, herein designated VGAM RNA, also designated SEQ ID:4423.

[57753] Another function of VGAM1712 is therefore inhibition of Heat Shock 70kDa Protein 9B (mortalin-2) (HSPA9B, Accession NM\_004134). Accordingly, utilities of VGAM1712



include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPA9B. Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM\_052966) is another VGAM1712 host target gene. C1orf24 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1orf24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf24 BINDING SITE, designated SEQ ID:27533, to the nucleotide sequence of VGAM1712 RNA, herein designated VGAM RNA, also designated SEQ ID:4423.

[57754] Another function of VGAM1712 is therefore inhibition of Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM\_052966). Accordingly, utilities of VGAM1712 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf24. NIBAN (Accession NM\_022083) is another VGAM1712 host target gene. NIBAN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NIBAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of NIBAN BINDING SITE, designated SEQ ID:22630, to the nucleotide sequence of VGAM1712 RNA, herein designated VGAM RNA, also designated SEQ ID:4423.

[57755] Another function of VGAM1712 is therefore inhibition of NIBAN (Accession NM\_022083). Accordingly, utilities of VGAM1712 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIBAN. Zinc Finger Protein 84 (HPF2) (ZNF84, Accession NM\_003428) is another VGAM1712 host target gene. ZNF84 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF84, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF84 BINDING SITE, designated SEQ ID:9479, to the nucleotide sequence of VGAM1712 RNA, herein designated VGAM RNA, also designated SEQ ID:4423.

[57756] Another function of VGAM1712 is therefore inhibition of Zinc Finger Protein 84 (HPF2) (ZNF84, Accession NM\_003428). Accordingly, utilities of VGAM1712 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIBAN.

cal conditions associated with ZNF84. LOC256310 (Accession XM\_172813) is another VGAM1712 host target gene. LOC256310 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC256310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256310 BINDING SITE, designated SEQ ID:46093, to the nucleotide sequence of VGAM1712 RNA, herein designated VGAM RNA, also designated SEQ ID:4423.

[57757] Another function of VGAM1712 is therefore inhibition of LOC256310 (Accession XM\_172813). Accordingly, utilities of VGAM1712 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256310. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1713 (VGAM1713) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57758] VGAM1713 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1713 was detected is described hereinabove with reference to Figs. 1–8.

[57759] VGAM1713 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sindbis Virus.

VGAM1713 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57760] VGAM1713 gene encodes a VGAM1713 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1713 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1713 precursor RNA is designated SEQ ID:1699, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1699 is located at position 8146 relative to the genome of Sindbis Virus.

[57761] VGAM1713 precursor RNA folds onto itself, forming VGAM1713 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57762] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1713 folded precursor RNA into VGAM1713 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1713 RNA is designated SEQ ID:4424, and is provided hereinbelow with reference to the sequence listing part.

[57763] VGAM1713 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1713 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1713 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57764] VGAM1713 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1713 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1713 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1713 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1713 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57765] The complementary binding of VGAM1713 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1713 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1713 host target RNA into VGAM1713 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57766] It is appreciated that VGAM1713 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1713 host target genes. The mRNA of each one of this plurality of VGAM1713 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1713 RNA, herein designated VGAM RNA, and which when bound by VGAM1713 RNA causes inhibition of translation of respective one or more VGAM1713 host target proteins.

[57767] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1713 gene, herein designated VGAM GENE, on one or more VGAM1713 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57768] It is yet further appreciated that a function of VGAM1713 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of viral infection by Sindbis Virus. Specific functions, and accordingly utilities, of VGAM1713 correlate with, and may be deduced from, the identity of the host target genes which VGAM1713 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57769] Nucleotide sequences of the VGAM1713 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the



`diced` VGAM1713 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1713 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1713 are further described hereinbelow with reference to Table 1.

[57770] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1713 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1713 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57771] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1713 gene, herein designated VGAM is inhibition of expression of VGAM1713 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1713 correlate with, and may be deduced from, the identity of the target genes which VGAM1713 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57772] ATP10C (Accession NM\_024490) is a VGAM1713 host target gene. ATP10C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by ATP10C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP10C BINDING SITE, designated SEQ ID:23687, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57773] A function of VGAM1713 is therefore inhibition of ATP10C (Accession NM\_024490), a gene which is phosphorylated in their intermediate state, drives uphill transport of ions across membranes. Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP10C. The function of ATP10C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM801. Phosphorylase Kinase, Beta (PHKB, Accession NM\_000293) is another VGAM1713 host target gene. PHKB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHKB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of PHKB BINDING SITE, designated SEQ ID:5837, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57774] Another function of VGAM1713 is therefore inhibition of Phosphorylase Kinase, Beta (PHKB, Accession NM\_000293). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHKB. Aminocarboxymuconate Semialdehyde Decarboxylase (acmsd, Accession NM\_138326) is another VGAM1713 host target gene. acmsd BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by acmsd, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of acmsd BINDING SITE, designated SEQ ID:28729, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57775] Another function of VGAM1713 is therefore inhibition of Aminocarboxymuconate Semialdehyde Decarboxylase (acmsd, Accession NM\_138326). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with acmsd. Angiomotin (AMOT, Accession NM\_133265) is another VGAM1713 host target gene. AMOT BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AMOT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOT BINDING SITE, designated SEQ ID:28411, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57776] Another function of VGAM1713 is therefore inhibition of Angiomotin (AMOT, Accession NM\_133265). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOT. Butyrophilin, Subfamily 2, Member A2 (BTN2A2, Accession NM\_006995) is another VGAM1713 host target gene. BTN2A2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BTN2A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN2A2 BINDING SITE,

designated SEQ ID:13858, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57777] Another function of VGAM1713 is therefore inhibition of Butyrophilin, Subfamily 2, Member A2 (BTN2A2, Accession NM\_006995). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN2A2. DKFZP564D0462 (Accession XM\_047080) is another VGAM1713 host target gene. DKFZP564D0462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564D0462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564D0462 BINDING SITE, designated SEQ ID:34897, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57778] Another function of VGAM1713 is therefore inhibition of DKFZP564D0462 (Accession XM\_047080). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D0462. Kv6.3 (Accession NM\_133490) is

another VGAM1713 host target gene. Kv6.3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Kv6.3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Kv6.3 BINDING SITE, designated SEQ ID:28565, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57779] Another function of VGAM1713 is therefore inhibition of Kv6.3 (Accession NM\_133490). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Kv6.3. LOC149153 (Accession XM\_097599) is another VGAM1713 host target gene. LOC149153 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149153 BINDING SITE, designated SEQ ID:40964, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57780] Another function of VGAM1713 is therefore inhibition of LOC149153 (Accession XM\_097599). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149153. LOC150759 (Accession XM\_086995) is another VGAM1713 host target gene. LOC150759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150759 BINDING SITE, designated SEQ ID:39012, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57781] Another function of VGAM1713 is therefore inhibition of LOC150759 (Accession XM\_086995). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150759. LOC151323 (Accession XM\_087168) is another VGAM1713 host target gene. LOC151323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151323, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151323 BINDING SITE, designated SEQ ID:39101, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57782] Another function of VGAM1713 is therefore inhibition of LOC151323 (Accession XM\_087168). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151323. LOC200399 (Accession XM\_114226) is another VGAM1713 host target gene. LOC200399 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200399 BINDING SITE, designated SEQ ID:42809, to the nucleotide sequence of VGAM1713 RNA, herein designated VGAM RNA, also designated SEQ ID:4424.

[57783] Another function of VGAM1713 is therefore inhibition of LOC200399 (Accession XM\_114226). Accordingly, utilities of VGAM1713 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC200399. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1714 (VGAM1714) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57784] VGAM1714 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1714 was detected is described hereinabove with reference to Figs. 1–8.

[57785] VGAM1714 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sindbis Virus. VGAM1714 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57786] VGAM1714 gene encodes a VGAM1714 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1714 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1714 precursor RNA is designated SEQ ID:1700, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1700 is located at position 9679 relative to the genome of Sindbis Virus.

- [57787] VGAM1714 precursor RNA folds onto itself, forming VGAM1714 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [57788] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1714 folded precursor RNA into VGAM1714 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1714 RNA is designated SEQ ID:4425, and is provided hereinbelow with reference to the sequence listing part.

[57789] VGAM1714 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1714 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1714 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57790] VGAM1714 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1714 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1714 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1714 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1714 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[57791] The complementary binding of VGAM1714 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1714 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1714 host target RNA into VGAM1714 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57792] It is appreciated that VGAM1714 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1714 host target genes. The mRNA of each one of this plurality of VGAM1714 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1714 RNA, herein designated VGAM RNA, and which when bound by VGAM1714 RNA causes

inhibition of translation of respective one or more VGAM1714 host target proteins.

[57793] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1714 gene, herein designated VGAM GENE, on one or more VGAM1714 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57794] It is yet further appreciated that a function of VGAM1714 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1714 include diagnosis, prevention and

treatment of viral infection by Sindbis Virus. Specific functions, and accordingly utilities, of VGAM1714 correlate with, and may be deduced from, the identity of the host target genes which VGAM1714 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57795] Nucleotide sequences of the VGAM1714 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1714 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1714 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1714 are further described hereinbelow with reference to Table 1.

[57796] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1714 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1714 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57797] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1714 gene, herein designated VGAM is inhibition of expression of VGAM1714 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1714 correlate with, and may be deduced from, the identity of the target genes which VGAM1714 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57798] Gamma-glutamyltransferase 2 (GGT2, Accession XM\_057166) is a VGAM1714 host target gene. GGT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GGT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGT2 BINDING SITE, designated SEQ ID:36486, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.

[57799] A function of VGAM1714 is therefore inhibition of Gamma-glutamyltransferase 2 (GGT2, Accession XM\_057166). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGT2. Gap Junction Protein, Beta 3, 31kDa (connexin 31) (GJB3, Accession NM\_024009) is another VGAM1714 host target gene. GJB3 BINDING SITE is HOST TARGET binding site found in the

3' untranslated region of mRNA encoded by GJB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GJB3 BINDING SITE, designated SEQ ID:23436, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.

[57800] Another function of VGAM1714 is therefore inhibition of Gap Junction Protein, Beta 3, 31kDa (connexin 31) (GJB3, Accession NM\_024009). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GJB3. Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM\_029962) is another VGAM1714 host target gene. KCNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNT1 BINDING SITE, designated SEQ ID:30971, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.



[57801] Another function of VGAM1714 is therefore inhibition of Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM\_029962). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNT1. KIAA0125 (Accession NM\_014792) is another VGAM1714 host target gene. KIAA0125 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0125, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0125 BINDING SITE, designated SEQ ID:16688, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.

[57802] Another function of VGAM1714 is therefore inhibition of KIAA0125 (Accession NM\_014792). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0125. KIAA0628 (Accession NM\_014789) is another VGAM1714 host target gene. KIAA0628 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0628, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0628 BINDING SITE, designated SEQ ID:16672, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.

[57803] Another function of VGAM1714 is therefore inhibition of KIAA0628 (Accession NM\_014789). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0628. SH3 Domain Binding Glutamic Acid-rich Protein Like (SH3BGRL, Accession XM\_030373) is another VGAM1714 host target gene. SH3BGRL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL BINDING SITE, designated SEQ ID:31026, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.

[57804] Another function of VGAM1714 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like

(SH3BGRL, Accession XM\_030373). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BGRL. LOC124602 (Accession XM\_058829) is another VGAM1714 host target gene. LOC124602 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124602, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124602 BINDING SITE, designated SEQ ID:36757, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.

[57805] Another function of VGAM1714 is therefore inhibition of LOC124602 (Accession XM\_058829). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124602. LOC149319 (Accession XM\_086495) is another VGAM1714 host target gene. LOC149319 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC149319 BINDING SITE, designated SEQ ID:38711, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.

[57806] Another function of VGAM1714 is therefore inhibition of LOC149319 (Accession XM\_086495). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149319. LOC203397 (Accession XM\_114695) is another VGAM1714 host target gene. LOC203397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203397 BINDING SITE, designated SEQ ID:43037, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.

[57807] Another function of VGAM1714 is therefore inhibition of LOC203397 (Accession XM\_114695). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203397. LOC254100 (Accession XM\_172851) is an-

other VGAM1714 host target gene. LOC254100 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254100 BINDING SITE, designated SEQ ID:46126, to the nucleotide sequence of VGAM1714 RNA, herein designated VGAM RNA, also designated SEQ ID:4425.

[57808] Another function of VGAM1714 is therefore inhibition of LOC254100 (Accession XM\_172851). Accordingly, utilities of VGAM1714 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254100. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1715 (VGAM1715) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57809] VGAM1715 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1715 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[57810] VGAM1715 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sindbis Virus.

VGAM1715 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57811] VGAM1715 gene encodes a VGAM1715 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1715 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1715 precursor RNA is designated SEQ ID:1701, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1701 is located at position 10643 relative to the genome of Sindbis Virus.

[57812] VGAM1715 precursor RNA folds onto itself, forming VGAM1715 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57813] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1715 folded precursor RNA into VGAM1715 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1715 RNA is designated SEQ ID:4426, and is provided hereinbelow with reference to the sequence listing part.

[57814] VGAM1715 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1715 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1715 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57815] VGAM1715 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1715 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1715 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1715 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1715 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57816] The complementary binding of VGAM1715 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1715 host target RNA, herein designated VGAM



HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1715 host target RNA into VGAM1715 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57817] It is appreciated that VGAM1715 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1715 host target genes. The mRNA of each one of this plurality of VGAM1715 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1715 RNA, herein designated VGAM RNA, and which when bound by VGAM1715 RNA causes inhibition of translation of respective one or more VGAM1715 host target proteins.

[57818] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1715 gene, herein designated VGAM GENE, on one or more VGAM1715 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57819] It is yet further appreciated that a function of VGAM1715 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1715 include diagnosis, prevention and treatment of viral infection by Sindbis Virus. Specific functions, and accordingly utilities, of VGAM1715 correlate with, and may be deduced from, the identity of the host target genes which VGAM1715 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57820] Nucleotide sequences of the VGAM1715 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1715 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1715 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1715 are further described hereinbelow with reference to Table 1.

[57821] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1715 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1715 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57822] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1715 gene, herein designated VGAM is inhibition of expression of VGAM1715 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1715 correlate with, and may be deduced from, the identity of the target genes which VGAM1715 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57823] Microtubule-associated Protein 1A (MAP1A, Accession NM\_002373) is a VGAM1715 host target gene. MAP1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP1A, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP1A BINDING SITE, designated SEQ ID:8183, to the nucleotide sequence of VGAM1715 RNA, herein designated VGAM RNA, also designated SEQ ID:4426.

[57824] A function of VGAM1715 is therefore inhibition of Microtubule-associated Protein 1A (MAP1A, Accession NM\_002373), a gene which is a structural protein involved in the filamentous cross-bridging between microtubules and other skeletal elements. Accordingly, utilities of VGAM1715 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP1A. The function of MAP1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM315. SORCS2 (Accession NM\_020777) is another VGAM1715 host target gene. SORCS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SORCS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORCS2 BINDING SITE, designated SEQ ID:21876, to the nucleotide

sequence of VGAM1715 RNA, herein designated VGAM RNA, also designated SEQ ID:4426.

[57825] Another function of VGAM1715 is therefore inhibition of SORCS2 (Accession NM\_020777). Accordingly, utilities of VGAM1715 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORCS2. DEPC-1 (Accession NM\_139178) is another VGAM1715 host target gene. DEPC-1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DEPC-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEPC-1 BINDING SITE, designated SEQ ID:29191, to the nucleotide sequence of VGAM1715 RNA, herein designated VGAM RNA, also designated SEQ ID:4426.

[57826] Another function of VGAM1715 is therefore inhibition of DEPC-1 (Accession NM\_139178). Accordingly, utilities of VGAM1715 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DEPC-1. FLJ12891 (Accession NM\_024950) is another VGAM1715 host target gene. FLJ12891 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ12891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12891 BINDING SITE, designated SEQ ID:24509, to the nucleotide sequence of VGAM1715 RNA, herein designated VGAM RNA, also designated SEQ ID:4426.

[57827] Another function of VGAM1715 is therefore inhibition of FLJ12891 (Accession NM\_024950). Accordingly, utilities of VGAM1715 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12891. FLJ21977 (Accession NM\_032213) is another VGAM1715 host target gene. FLJ21977 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21977 BINDING SITE, designated SEQ ID:25939, to the nucleotide sequence of VGAM1715 RNA, herein designated VGAM RNA, also designated SEQ ID:4426.

[57828] Another function of VGAM1715 is therefore inhibition of FLJ21977 (Accession NM\_032213). Accordingly, utilities of

VGAM1715 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21977. Protein Phosphatase 2 (formerly 2A), Regulatory Subunit B", Alpha (PPP2R3A, Accession NM\_002718) is another VGAM1715 host target gene. PPP2R3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP2R3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R3A BINDING SITE, designated SEQ ID:8585, to the nucleotide sequence of VGAM1715 RNA, herein designated VGAM RNA, also designated SEQ ID:4426.

[57829] Another function of VGAM1715 is therefore inhibition of Protein Phosphatase 2 (formerly 2A), Regulatory Subunit B", Alpha (PPP2R3A, Accession NM\_002718). Accordingly, utilities of VGAM1715 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R3A. LOC146108 (Accession XM\_085322) is another VGAM1715 host target gene. LOC146108 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146108, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146108 BINDING SITE, designated SEQ ID:38062, to the nucleotide sequence of VGAM1715 RNA, herein designated VGAM RNA, also designated SEQ ID:4426.

[57830] Another function of VGAM1715 is therefore inhibition of LOC146108 (Accession XM\_085322). Accordingly, utilities of VGAM1715 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146108. LOC219529 (Accession XM\_167563) is another VGAM1715 host target gene. LOC219529 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219529 BINDING SITE, designated SEQ ID:44671, to the nucleotide sequence of VGAM1715 RNA, herein designated VGAM RNA, also designated SEQ ID:4426.

[57831] Another function of VGAM1715 is therefore inhibition of LOC219529 (Accession XM\_167563). Accordingly, utilities of VGAM1715 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC219529. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1716 (VGAM1716) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57832] VGAM1716 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1716 was detected is described hereinabove with reference to Figs. 1–8.

[57833] VGAM1716 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sindbis Virus. VGAM1716 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57834] VGAM1716 gene encodes a VGAM1716 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1716 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1716 precursor RNA is designated SEQ ID:1702, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1702 is located at position 8996 relative to the genome of Sindbis Virus.

- [57835] VGAM1716 precursor RNA folds onto itself, forming VGAM1716 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [57836] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1716 folded precursor RNA into VGAM1716 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1716 RNA is designated SEQ ID:4427, and is provided hereinbelow with reference to the sequence listing part.

[57837] VGAM1716 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1716 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1716 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57838] VGAM1716 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1716 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1716 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1716 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1716 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57839] The complementary binding of VGAM1716 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1716 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1716 host target RNA into VGAM1716 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57840] It is appreciated that VGAM1716 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1716 host target genes. The mRNA of each one of this plurality of VGAM1716 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1716 RNA, herein designated VGAM RNA, and which when bound by VGAM1716 RNA causes

inhibition of translation of respective one or more VGAM1716 host target proteins.

[57841] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1716 gene, herein designated VGAM GENE, on one or more VGAM1716 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57842] It is yet further appreciated that a function of VGAM1716 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1716 include diagnosis, prevention and

treatment of viral infection by Sindbis Virus. Specific functions, and accordingly utilities, of VGAM1716 correlate with, and may be deduced from, the identity of the host target genes which VGAM1716 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57843] Nucleotide sequences of the VGAM1716 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1716 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1716 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1716 are further described hereinbelow with reference to Table 1.

[57844] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1716 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1716 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57845] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1716 gene, herein designated VGAM is inhibition of expression of VGAM1716 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1716 correlate with, and may be deduced from, the identity of the target genes which VGAM1716 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57846] Membrane Cofactor Protein (CD46, trophoblast-lymphocyte cross-reactive antigen) (MCP, Accession NM\_002389) is a VGAM1716 host target gene. MCP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MCP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCP BINDING SITE, designated SEQ ID:8205, to the nucleotide sequence of VGAM1716 RNA, herein designated VGAM RNA, also designated SEQ ID:4427.

[57847] A function of VGAM1716 is therefore inhibition of Membrane Cofactor Protein (CD46, trophoblast-lymphocyte cross-reactive antigen) (MCP, Accession NM\_002389), a gene which may be involved in the regulation of complement activation. Accordingly, utilities of VGAM1716 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCP. The function of

MCP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM383.DKFZP564C196 (Accession XM\_046405) is another VGAM1716 host target gene. DKFZP564C196 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564C196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564C196 BINDING SITE, designated SEQ ID:34715, to the nucleotide sequence of VGAM1716 RNA, herein designated VGAM RNA, also designated SEQ ID:4427.

[57848] Another function of VGAM1716 is therefore inhibition of DKFZP564C196 (Accession XM\_046405). Accordingly, utilities of VGAM1716 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564C196. FLJ20984 (Accession NM\_024630) is another VGAM1716 host target gene. FLJ20984 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20984, corresponding to a HOST TARGET binding site such as BINDING



SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20984 BINDING SITE, designated SEQ ID:23895, to the nucleotide sequence of VGAM1716 RNA, herein designated VGAM RNA, also designated SEQ ID:4427.

[57849] Another function of VGAM1716 is therefore inhibition of FLJ20984 (Accession NM\_024630). Accordingly, utilities of VGAM1716 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20984. Zinc Finger Protein 95 Homolog (mouse) (ZFP95, Accession NM\_014569) is another VGAM1716 host target gene. ZFP95 BINDING SITE1 and ZFP95 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ZFP95, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP95 BINDING SITE1 and ZFP95 BINDING SITE2, designated SEQ ID:15918 and SEQ ID:29708 respectively, to the nucleotide sequence of VGAM1716 RNA, herein designated VGAM RNA, also designated SEQ ID:4427.

[57850] Another function of VGAM1716 is therefore inhibition of Zinc Finger Protein 95 Homolog (mouse) (ZFP95, Acces-

sion NM\_014569). Accordingly, utilities of VGAM1716 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP95. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1717 (VGAM1717) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57851] VGAM1717 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1717 was detected is described hereinabove with reference to Figs. 1-8.

[57852] VGAM1717 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum Contagiosum Virus. VGAM1717 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57853] VGAM1717 gene encodes a VGAM1717 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1717 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1717 precursor RNA is designated SEQ ID:1703, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1703 is located at position 67026 relative to the genome of Molluscum Contagiosum Virus.

- [57854] VGAM1717 precursor RNA folds onto itself, forming VGAM1717 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [57855] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1717 folded precursor RNA into VGAM1717 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1717 RNA is designated SEQ ID:4428, and

is provided hereinbelow with reference to the sequence listing part.

[57856] VGAM1717 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1717 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1717 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57857] VGAM1717 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1717 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1717 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1717 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1717 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57858] The complementary binding of VGAM1717 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1717 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1717 host target RNA into VGAM1717 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57859] It is appreciated that VGAM1717 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1717 host target genes. The mRNA of each one of this plurality of VGAM1717 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1717 RNA, herein designated VGAM RNA, and which when bound by VGAM1717 RNA causes inhibition of translation of respective one or more VGAM1717 host target proteins.

[57860] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1717 gene, herein designated VGAM GENE, on one or more VGAM1717 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57861] It is yet further appreciated that a function of VGAM1717 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1717 include diagnosis, prevention and treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGAM1717 correlate with, and may be deduced from, the identity of the host target genes which VGAM1717 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57862] Nucleotide sequences of the VGAM1717 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1717 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1717 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1717 are further described hereinbelow with reference to Table 1.

[57863] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1717 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1717 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57864] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1717 gene, herein designated VGAM is inhibition of expression of VGAM1717 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1717 correlate with, and may be deduced from, the identity of the target genes which VGAM1717 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57865] Adenosine Deaminase, RNA-specific, B1 (RED1 homolog rat) (ADARB1, Accession NM\_001112) is a VGAM1717 host target gene. ADARB1 BINDING SITE1 and ADARB1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADARB1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADARB1 BINDING SITE1 and ADARB1 BINDING SITE2, designated SEQ ID:6777 and SEQ ID:17948 respectively, to the nucleotide sequence of VGAM1717 RNA, herein designated VGAM RNA, also designated SEQ ID:4428.

[57866] A function of VGAM1717 is therefore inhibition of Adenosine Deaminase, RNA-specific, B1 (RED1 homolog rat) (ADARB1, Accession NM\_001112), a gene which RNA editing involves the deamination of adenosines at specific



sites. Accordingly, utilities of VGAM1717 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADARB1. The function of ADARB1 has been established by previous studies. RNA editing involves the deamination of adenosines at specific sites, the result of which can be a change in the amino acid sequence of the protein so that it differs from that predicted by the sequence of the DNA. Editing of the glutamate receptor B (GluRB; 138247) pre-mRNA has been shown to alter a codon (referred to as the Q/R site) for a channel determinant that controls the calcium permeability of the AMPA glutamate receptors. Melcher et al. (1996) tested the candidate dsRNA adenosine deaminase DRADA (OMIM Ref. No. 601059) and showed that when coexpressed with a GluR-B minigene in HEK 293 cells, DRADA produced low-level editing at the GluR-B Q/R site. The authors then screened a rat brain cDNA library with the predicted catalytic domain of rat DRADA to identify other potential editing enzymes. A cDNA encoding a predicted 711-amino acid protein was isolated that gave about 90% of the expected activity in their editing assay. Melcher et al. (1996) designated this novel mammalian RNA editing protein RNA-editing enzyme-1 (RED1). Rat RED1 and

DRADA share about 31% overall identity primarily due to their conservation in the C-terminal catalytic domain. Northern blots showed highest expression of RED1 in rat brain. Melcher et al. (1996) further observed that while RED1 was more efficient at deaminating some sites, DRADA had stronger activity at others. They speculated that a combination of these and perhaps other editing enzymes may be involved in determining the overall editing process for a given transcript. Higuchi et al. (2000) studied ADAR2-mediated RNA editing by generating mice that were homozygous for a targeted functional null allele. Editing in *Adar2*  $-/-$  mice was substantially reduced at most of 25 positions in diverse transcripts; the mutant mice became prone to seizures and died young. The impaired phenotype appeared to result entirely from a single underedited position, since it reverted to normal when both alleles for the underedited transcript were substituted with alleles encoding the edited version exonically. The critical position specifies an ion channel determinant, the Q/R site, in AMPA receptor GluRB premessenger RNA. Higuchi et al. (2000) concluded that this transcript is physiologically the most important substrate of ADAR2.

[57867] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [57868] Melcher, T.; Maas, S.; Herb, A.; Sprengel, R.; Seeburg, P. H.; Higuchi, M. : A mammalian RNA editing enzyme. Nature 379: 460–463, 1996. ; and
- [57869] Higuchi, M.; Maas, S.; Single, F. N.; Hartner, J.; Rozov, A.; Burnashev, N.; Feldmeyer, D.; Sprengel, R.; Seeburg, P. H. : Point mutation in an AMPA receptor gene rescues lethality in mi.
- [57870] Further studies establishing the function and utilities of ADARB1 are found in John Hopkins OMIM database record ID 601218, and in cited publications numbered 7167–7173 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ14566 (Accession NM\_032806) is another VGAM1717 host target gene. FLJ14566 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14566 BINDING SITE, designated SEQ ID:26564, to the nucleotide sequence of VGAM1717 RNA, herein designated VGAM RNA, also designated SEQ

ID:4428.

[57871] Another function of VGAM1717 is therefore inhibition of FLJ14566 (Accession NM\_032806). Accordingly, utilities of VGAM1717 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14566. KIAA1644 (Accession XM\_097892) is another VGAM1717 host target gene. KIAA1644 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1644 BINDING SITE, designated SEQ ID:41200, to the nucleotide sequence of VGAM1717 RNA, herein designated VGAM RNA, also designated SEQ ID:4428.

[57872] Another function of VGAM1717 is therefore inhibition of KIAA1644 (Accession XM\_097892). Accordingly, utilities of VGAM1717 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1644. RoXaN (Accession NM\_025013) is another VGAM1717 host target gene. RoXaN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RoXaN, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RoXaN BINDING SITE, designated SEQ ID:24600, to the nucleotide sequence of VGAM1717 RNA, herein designated VGAM RNA, also designated SEQ ID:4428.

[57873] Another function of VGAM1717 is therefore inhibition of RoXaN (Accession NM\_025013). Accordingly, utilities of VGAM1717 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RoXaN. LOC128989 (Accession XM\_059310) is another VGAM1717 host target gene. LOC128989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128989 BINDING SITE, designated SEQ ID:36939, to the nucleotide sequence of VGAM1717 RNA, herein designated VGAM RNA, also designated SEQ ID:4428.

[57874] Another function of VGAM1717 is therefore inhibition of LOC128989 (Accession XM\_059310). Accordingly, utilities of VGAM1717 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC128989. LOC147054 (Accession XM\_097172) is another VGAM1717 host target gene. LOC147054 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC147054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147054 BINDING SITE, designated SEQ ID:40788, to the nucleotide sequence of VGAM1717 RNA, herein designated VGAM RNA, also designated SEQ ID:4428.

[57875] Another function of VGAM1717 is therefore inhibition of LOC147054 (Accession XM\_097172). Accordingly, utilities of VGAM1717 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147054. LOC149103 (Accession XM\_086434) is another VGAM1717 host target gene. LOC149103 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149103 BINDING SITE, designated SEQ ID:38651, to

the nucleotide sequence of VGAM1717 RNA, herein designated VGAM RNA, also designated SEQ ID:4428.

[57876] Another function of VGAM1717 is therefore inhibition of LOC149103 (Accession XM\_086434). Accordingly, utilities of VGAM1717 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149103. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1718 (VGAM1718) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57877] VGAM1718 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1718 was detected is described hereinabove with reference to Figs. 1–8.

[57878] VGAM1718 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum Contagiosum Virus. VGAM1718 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57879] VGAM1718 gene encodes a VGAM1718 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1718 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1718 precursor RNA is designated SEQ ID:1704, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1704 is located at position 64920 relative to the genome of Molluscum Contagiosum Virus.

[57880] VGAM1718 precursor RNA folds onto itself, forming VGAM1718 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57881] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1718 folded precursor RNA into VGAM1718 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1718 RNA is designated SEQ ID:4429, and is provided hereinbelow with reference to the sequence listing part.

[57882] VGAM1718 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1718 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1718 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57883] VGAM1718 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1718 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1718 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1718 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1718 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57884] The complementary binding of VGAM1718 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1718 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1718 host target RNA into VGAM1718 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57885] It is appreciated that VGAM1718 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1718 host target genes. The mRNA of each one of this plurality of VGAM1718 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1718 RNA, herein designated VGAM RNA, and which when bound by VGAM1718 RNA causes inhibition of translation of respective one or more VGAM1718 host target proteins.

[57886] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1718 gene, herein designated VGAM GENE, on one or more VGAM1718 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[57887] It is yet further appreciated that a function of VGAM1718 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGAM1718 correlate with, and may be deduced from, the identity of the host target genes which VGAM1718 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57888] Nucleotide sequences of the VGAM1718 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1718 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1718 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1718 are further described hereinbelow with reference to Table 1.

[57889] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1718 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1718 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57890] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1718 gene, herein designated VGAM is inhibition of expression of VGAM1718 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1718 correlate with, and may be deduced from, the identity of the target genes which VGAM1718 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57891] Aquaporin 1 (channel-forming integral protein, 28kDa) (AQP1, Accession NM\_000385) is a VGAM1718 host target gene. AQP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AQP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP1 BINDING SITE, designated SEQ ID:5958, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57892] A function of VGAM1718 is therefore inhibition of Aquaporin 1 (channel-forming integral protein, 28kDa) (AQP1,

Accession NM\_000385). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AQP1. ATPase, Aminophospholipid Transporter-like, Class I, Type 8A, Member 2 (ATP8A2, Accession XM\_167916) is another VGAM1718 host target gene. ATP8A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP8A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8A2 BINDING SITE, designated SEQ ID:44919, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57893] Another function of VGAM1718 is therefore inhibition of ATPase, Aminophospholipid Transporter-like, Class I, Type 8A, Member 2 (ATP8A2, Accession XM\_167916). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8A2. Delta-like 1 Homolog (Drosophila) (DLK1, Accession NM\_003836) is another VGAM1718 host target gene. DLK1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by DLK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLK1 BINDING SITE, designated SEQ ID:9928, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57894] Another function of VGAM1718 is therefore inhibition of Delta-like 1 Homolog (Drosophila) (DLK1, Accession NM\_003836), a gene which may have a role in neuroendocrine differentiation. Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLK1. The function of DLK1 has been established by previous studies. Lee et al. (1995) reported that DLK, pG2, and PREF1 are variant products of the same gene. They noted that C. Smas and H.S. Sul acknowledged in a personal communication that the major point of divergence between mouse Dlk and Pref1 was due to sequence data misinterpretation. Sequence analysis of multiple human DLK cDNAs revealed that there are several variant forms of DLK mRNA. Dlk1 and Gtl2 (OMIM Ref. No. 605636) are reciprocally imprinted genes located 80 kb apart on mouse chromosome

12. There are similarities between this domain and that of the well-characterized Igf2/H19 locus (see OMIM Ref. No. 103280) (Wylie et al., 2000). Takada et al. (2002) described a detailed methylation analysis of the Dlk1/Gtl2 domain on both parental alleles in the mouse. Like the Igf2/H19 domain, areas of differential methylation are hypermethylated on the paternal allele and hypomethylated on the maternal allele. Three differentially methylated regions (DMRs), each with different epigenetic characteristics, were identified. One DMR is intergenic, contains tandem repeats, and is the only region that inherits a paternal methylation mark from the germline. An intronic DMR contains a conserved putative CTCF (OMIM Ref. No. 604167)-binding domain. All 3 DMRs have both unique and common features compared to those identified in the Igf2/H19 domain.

[57895] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57896] Jensen, C. H.; Krogh, T. N.; Hojrup, P.; Clausen, P. P.; Skjodt, K.; Larsson, L.-I.; Enghild, J. J.; Teisner, B. : Protein structure of fetal antigen 1 (FA1): a novel circulating human epidermal-growth-factor-like protein expressed in



neuroendocrine tumors and its relation to the gene products of dlk and pG2. *Europ. J. Biochem.* 225: 83–92, 1994.  
; and

[57897] Takada, S.; Paulsen, M.; Tevendale, M.; Tsai, C.–E.; Kelsey, G.; Cattanach, B. M.; Ferguson–Smith, A. C. : Epigenetic analysis of the Dlk1–Gtl2 imprinted domain on mouse chromosome 12: i.

[57898] Further studies establishing the function and utilities of DLK1 are found in John Hopkins OMIM database record ID 176290, and in cited publications numbered 49–50, 54, 70 and 5459–5462 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Huntingtin (Huntington disease) (HD, Accession NM\_002111) is another VGAM1718 host target gene. HD BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HD BINDING SITE, designated SEQ ID:7892, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57899] Another function of VGAM1718 is therefore inhibition of

Huntingtin (Huntington disease) (HD, Accession NM\_002111). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HD. Interleukin 12 Receptor, Beta 2 (IL12RB2, Accession NM\_001559) is another VGAM1718 host target gene. IL12RB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL12RB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL12RB2 BINDING SITE, designated SEQ ID:7278, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57900] Another function of VGAM1718 is therefore inhibition of Interleukin 12 Receptor, Beta 2 (IL12RB2, Accession NM\_001559), a gene which is involved in il-12 transduction. binds to il-12 with a low affinity. Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL12RB2. The function of IL12RB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM326.Jagged 2 (JAG2, Accession NM\_002226) is another VGAM1718 host target gene. JAG2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by JAG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAG2 BINDING SITE, designated SEQ ID:8004, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57901] Another function of VGAM1718 is therefore inhibition of Jagged 2 (JAG2, Accession NM\_002226), a gene which is a putative notch ligand involved in the mediation of notch signaling. Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAG2. The function of JAG2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM136.Msh Homeo Box Homolog 1 (Drosophila) (MSX1, Accession NM\_002448) is another VGAM1718 host target gene. MSX1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MSX1,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSX1 BINDING SITE, designated SEQ ID:8286, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57902] Another function of VGAM1718 is therefore inhibition of Msh Homeo Box Homolog 1 (Drosophila) (MSX1, Accession NM\_002448). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSX1. Metastasis-associated 1-like 1 (MTA1L1, Accession NM\_004739) is another VGAM1718 host target gene. MTA1L1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MTA1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTA1L1 BINDING SITE, designated SEQ ID:11135, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57903] Another function of VGAM1718 is therefore inhibition of Metastasis-associated 1-like 1 (MTA1L1, Accession

NM\_004739), a gene which regulates histone deacetylase core complex enzymatic activity. Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTA1L1. The function of MTA1L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM659. Myotubularin Related Protein 3 (MTMR3, Accession NM\_021090) is another VGAM1718 host target gene. MTMR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTMR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR3 BINDING SITE, designated SEQ ID:22073, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57904] Another function of VGAM1718 is therefore inhibition of Myotubularin Related Protein 3 (MTMR3, Accession NM\_021090), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with MTMR3. The function of MTMR3 has been established by previous studies. Zhao et al. (2001) showed that an isoform of MTMR3, missing exon 17, dephosphorylates para-nitrophenylphosphate and phosphatidylinositol 3-phosphate.

[57905] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[57906] Nagase, T.; Ishikawa, K.; Nakajima, D.; Ohira, M.; Seki, N.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. VII. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro. DNA Res. 4: 141-150, 1997. ; and

[57907] Zhao, R.; Qi, Y.; Chen, J.; Zhao, Z. J. : FYVE-DSP2, a FYVE domain-containing dual specificity protein phosphatase that dephosphorylates phosphotidylinositol (sic) 3-phosphate. Exp. Cel.

[57908] Further studies establishing the function and utilities of MTMR3 are found in John Hopkins OMIM database record ID 603558, and in cited publications numbered 725 and 5003 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Phos-

phatase 2 (formerly 2A), Regulatory Subunit B (PR 52), Gamma Isoform (PPP2R2C, Accession XM\_029744) is another VGAM1718 host target gene. PPP2R2C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPP2R2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R2C BINDING SITE, designated SEQ ID:30939, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57909] Another function of VGAM1718 is therefore inhibition of Protein Phosphatase 2 (formerly 2A), Regulatory Subunit B (PR 52), Gamma Isoform (PPP2R2C, Accession XM\_029744). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R2C. Solute Carrier Family 19 (folate transporter), Member 1 (SLC19A1, Accession NM\_003056) is another VGAM1718 host target gene. SLC19A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC19A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SLC19A1 BINDING SITE, designated SEQ ID:9020, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57910] Another function of VGAM1718 is therefore inhibition of Solute Carrier Family 19 (folate transporter), Member 1 (SLC19A1, Accession NM\_003056). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC19A1. Tripartite Motif-containing 9 (TRIM9, Accession NM\_015163) is another VGAM1718 host target gene. TRIM9 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TRIM9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM9 BINDING SITE, designated SEQ ID:17518, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57911] Another function of VGAM1718 is therefore inhibition of Tripartite Motif-containing 9 (TRIM9, Accession



NM\_015163), a gene which may function as a positive regulator for mannosylphosphate transferase and is required to mediate mannosylphosphate transfer in both the core and outer chain portions of n-linked oligosaccharides. Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM9. The function of TRIM9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Transient Receptor Potential Cation Channel, Subfamily V, Member 2 (TRPV2, Accession NM\_016113) is another VGAM1718 host target gene. TRPV2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPV2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPV2 BINDING SITE, designated SEQ ID:18195, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57912] Another function of VGAM1718 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily V,

Member 2 (TRPV2, Accession NM\_016113). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPV2. Ubiquitin Specific Protease 6 (Tre-2 oncogene) (USP6, Accession XM\_165948) is another VGAM1718 host target gene. USP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by USP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP6 BINDING SITE, designated SEQ ID:43807, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57913] Another function of VGAM1718 is therefore inhibition of Ubiquitin Specific Protease 6 (Tre-2 oncogene) (USP6, Accession XM\_165948), a gene which has an atp-independent isopeptidase activity, cleaving at the carboxyl terminus of the ubiquitin moiety. Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP6. The function of USP6 and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM296.C1q and Tumor Necrosis Factor Related Protein 7 (C1QTNF7, Accession NM\_031911) is another VGAM1718 host target gene. C1QTNF7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1QTNF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QTNF7 BINDING SITE, designated SEQ ID:25662, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57914] Another function of VGAM1718 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 7 (C1QTNF7, Accession NM\_031911). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF7. Chromobox Homolog 6 (CBX6, Accession NM\_014292) is another VGAM1718 host target gene. CBX6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CBX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of CBX6 BINDING SITE, designated SEQ ID:15572, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57915] Another function of VGAM1718 is therefore inhibition of Chromobox Homolog 6 (CBX6, Accession NM\_014292). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX6. DKFZP434O047 (Accession NM\_015594) is another VGAM1718 host target gene. DKFZP434O047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434O047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434O047 BINDING SITE, designated SEQ ID:17860, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57916] Another function of VGAM1718 is therefore inhibition of DKFZP434O047 (Accession NM\_015594). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZP434O047. DR1-associated Protein 1 (negative cofactor 2 alpha) (DRAP1, Accession NM\_006442) is another VGAM1718 host target gene. DRAP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DRAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRAP1 BINDING SITE, designated SEQ ID:13154, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57917] Another function of VGAM1718 is therefore inhibition of DR1-associated Protein 1 (negative cofactor 2 alpha) (DRAP1, Accession NM\_006442). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRAP1. FLJ00001 (Accession XM\_088525) is another VGAM1718 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ00001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00001 BINDING SITE,

designated SEQ ID:39779, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57918] Another function of VGAM1718 is therefore inhibition of FLJ00001 (Accession XM\_088525). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00001. FLJ21562 (Accession NM\_025113) is another VGAM1718 host target gene. FLJ21562 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21562, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21562 BINDING SITE, designated SEQ ID:24761, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57919] Another function of VGAM1718 is therefore inhibition of FLJ21562 (Accession NM\_025113). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21562. KIAA0350 (Accession XM\_028332) is another VGAM1718 host target gene. KIAA0350 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0350 BINDING SITE, designated SEQ ID:30658, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57920] Another function of VGAM1718 is therefore inhibition of KIAA0350 (Accession XM\_028332). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0350. KIAA0513 (Accession NM\_014732) is another VGAM1718 host target gene. KIAA0513 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0513 BINDING SITE, designated SEQ ID:16351, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57921] Another function of VGAM1718 is therefore inhibition of

KIAA0513 (Accession NM\_014732). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0513. KIAA1297 (Accession XM\_051005) is another VGAM1718 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35714, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57922] Another function of VGAM1718 is therefore inhibition of KIAA1297 (Accession XM\_051005). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. KIAA1813 (Accession XM\_046743) is another VGAM1718 host target gene. KIAA1813 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the



complementarity of the nucleotide sequences of KIAA1813 BINDING SITE, designated SEQ ID:34813, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57923] Another function of VGAM1718 is therefore inhibition of KIAA1813 (Accession XM\_046743). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1813. KIAA1977 (Accession XM\_058800) is another VGAM1718 host target gene. KIAA1977 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1977 BINDING SITE, designated SEQ ID:36748, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57924] Another function of VGAM1718 is therefore inhibition of KIAA1977 (Accession XM\_058800). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1977. MOT8 (Accession NM\_018836) is another

VGAM1718 host target gene. MOT8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOT8 BINDING SITE, designated SEQ ID:20823, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57925] Another function of VGAM1718 is therefore inhibition of MOT8 (Accession NM\_018836). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOT8. Obscurin, Cytoskeletal Calmodulin and Titin-interacting RhoGEF (OBSCN, Accession XM\_047536) is another VGAM1718 host target gene. OBSCN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OBSCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OBSCN BINDING SITE, designated SEQ ID:34990, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA,

also designated SEQ ID:4429.

[57926] Another function of VGAM1718 is therefore inhibition of Obscurin, Cytoskeletal Calmodulin and Titin-interacting RhoGEF (OBSCN, Accession XM\_047536). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OBSCN. Retinoic Acid Induced 16 (RAI16, Accession NM\_022749) is another VGAM1718 host target gene. RAI16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI16 BINDING SITE, designated SEQ ID:22968, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57927] Another function of VGAM1718 is therefore inhibition of Retinoic Acid Induced 16 (RAI16, Accession NM\_022749). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI16. RHO6 (Accession NM\_014470) is another VGAM1718 host target gene. RHO6 BINDING SITE is HOST TARGET binding site found in

the 3` untranslated region of mRNA encoded by RHO6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHO6 BINDING SITE, designated SEQ ID:15820, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57928] Another function of VGAM1718 is therefore inhibition of RHO6 (Accession NM\_014470). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHO6. LOC125704 (Accession XM\_058931) is another VGAM1718 host target gene. LOC125704 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC125704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC125704 BINDING SITE, designated SEQ ID:36796, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57929] Another function of VGAM1718 is therefore inhibition of LOC125704 (Accession XM\_058931). Accordingly, utilities

of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC125704. LOC126917 (Accession XM\_059091) is another VGAM1718 host target gene. LOC126917 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC126917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126917 BINDING SITE, designated SEQ ID:36869, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57930] Another function of VGAM1718 is therefore inhibition of LOC126917 (Accession XM\_059091). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126917. LOC146782 (Accession XM\_083963) is another VGAM1718 host target gene. LOC146782 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC146782 BINDING SITE, designated SEQ ID:37523, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57931] Another function of VGAM1718 is therefore inhibition of LOC146782 (Accession XM\_083963). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146782. LOC152078 (Accession XM\_087376) is another VGAM1718 host target gene. LOC152078 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152078 BINDING SITE, designated SEQ ID:39212, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57932] Another function of VGAM1718 is therefore inhibition of LOC152078 (Accession XM\_087376). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152078. LOC200014 (Accession XM\_114087) is another VGAM1718 host target gene. LOC200014 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200014 BINDING SITE, designated SEQ ID:42688, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57933] Another function of VGAM1718 is therefore inhibition of LOC200014 (Accession XM\_114087). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200014. LOC255397 (Accession XM\_173868) is another VGAM1718 host target gene. LOC255397 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255397 BINDING SITE, designated SEQ ID:46565, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57934] Another function of VGAM1718 is therefore inhibition of

LOC255397 (Accession XM\_173868). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255397. LOC256158 (Accession XM\_175125) is another VGAM1718 host target gene. LOC256158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE, designated SEQ ID:46616, to the nucleotide sequence of VGAM1718 RNA, herein designated VGAM RNA, also designated SEQ ID:4429.

[57935] Another function of VGAM1718 is therefore inhibition of LOC256158 (Accession XM\_175125). Accordingly, utilities of VGAM1718 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256158. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1719 (VGAM1719) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes



is known in the art.

[57936] VGAM1719 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1719 was detected is described hereinabove with reference to Figs. 1–8.

[57937] VGAM1719 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat Cytomegalovirus. VGAM1719 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57938] VGAM1719 gene encodes a VGAM1719 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1719 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1719 precursor RNA is designated SEQ ID:1705, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1705 is located at position 110474 relative to the genome of Rat Cytomegalovirus.

[57939] VGAM1719 precursor RNA folds onto itself, forming VGAM1719 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57940] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1719 folded precursor RNA into VGAM1719 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1719 RNA is designated SEQ ID:4430, and is provided hereinbelow with reference to the sequence listing part.

[57941] VGAM1719 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1719 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1719 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[57942] VGAM1719 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1719 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1719 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1719 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1719 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[57943] The complementary binding of VGAM1719 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1719 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1719 host target RNA into VGAM1719 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57944] It is appreciated that VGAM1719 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1719 host target genes. The mRNA of each one of this plurality of VGAM1719 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1719 RNA, herein designated VGAM RNA, and which when bound by VGAM1719 RNA causes inhibition of translation of respective one or more VGAM1719 host target proteins.

[57945] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1719 gene, herein designated VGAM GENE, on one

or more VGAM1719 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57946] It is yet further appreciated that a function of VGAM1719 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of viral infection by Rat Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1719 correlate with, and may be deduced from, the identity of the host target genes which VGAM1719 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57947] Nucleotide sequences of the VGAM1719 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1719 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1719 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1719 are further described hereinbelow with reference to Table 1.

[57948] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1719 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1719 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57949] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1719 gene, herein designated VGAM is inhibition of expression of VGAM1719 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1719 correlate with, and may be deduced from, the identity of the target genes which VGAM1719 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57950] PYGO2 (Accession XM\_034083) is a VGAM1719 host tar-

get gene. PYGO2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PYGO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYGO2 BINDING SITE, designated SEQ ID:31999, to the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57951] A function of VGAM1719 is therefore inhibition of PYGO2 (Accession XM\_034083). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYGO2. Suppression of Tumorigenicity 7 (ST7, Accession NM\_018412) is another VGAM1719 host target gene. ST7 BINDING SITE1 and ST7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ST7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST7 BINDING SITE1 and ST7 BINDING SITE2, designated SEQ ID:20455 and SEQ ID:22431 respectively, to the nucleotide sequence of VGAM1719

RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57952] Another function of VGAM1719 is therefore inhibition of Suppression of Tumorigenicity 7 (ST7, Accession NM\_018412), a gene which has a role in regulating cell–environment or cell–cell interactions. Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST7. The function of ST7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107.DKFZp434O0515 (Accession XM\_038277) is another VGAM1719 host target gene. DKFZp434O0515 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp434O0515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434O0515 BINDING SITE, designated SEQ ID:32786, to the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57953] Another function of VGAM1719 is therefore inhibition of



DKFZp434O0515 (Accession XM\_038277). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434O0515. KIAA1161 (Accession XM\_088501) is another VGAM1719 host target gene. KIAA1161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1161 BINDING SITE, designated SEQ ID:39753, to the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57954] Another function of VGAM1719 is therefore inhibition of KIAA1161 (Accession XM\_088501). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1161. MAD, Mothers Against Decapentaplegic Homolog (Drosophila) Interacting Protein, Receptor Activation Anchor (MADHIP, Accession NM\_007323) is another VGAM1719 host target gene. MADHIP BINDING SITE1 through MADHIP BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

MADHIP, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADHIP BINDING SITE1 through MADHIP BINDING SITE3, designated SEQ ID:14241, SEQ ID:14243 and SEQ ID:11220 respectively, to the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57955] Another function of VGAM1719 is therefore inhibition of MAD, Mothers Against Decapentaplegic Homolog (Drosophila) Interacting Protein, Receptor Activation Anchor (MADHIP, Accession NM\_007323). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADHIP. LOC124216 (Accession XM\_058783) is another VGAM1719 host target gene. LOC124216 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124216, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124216 BINDING SITE, designated SEQ ID:36739, to the nucleotide sequence of VGAM1719 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4430.

[57956] Another function of VGAM1719 is therefore inhibition of LOC124216 (Accession XM\_058783). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124216. LOC147071 (Accession XM\_054031) is another VGAM1719 host target gene. LOC147071 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147071 BINDING SITE, designated SEQ ID:36137, to the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57957] Another function of VGAM1719 is therefore inhibition of LOC147071 (Accession XM\_054031). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147071. LOC201173 (Accession XM\_113312) is another VGAM1719 host target gene. LOC201173 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201173, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201173 BINDING SITE, designated SEQ ID:42216, to the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57958] Another function of VGAM1719 is therefore inhibition of LOC201173 (Accession XM\_113312). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201173. LOC201220 (Accession XM\_113321) is another VGAM1719 host target gene. LOC201220 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201220 BINDING SITE, designated SEQ ID:42223, to the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57959] Another function of VGAM1719 is therefore inhibition of LOC201220 (Accession XM\_113321). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC201220. LOC203504 (Accession XM\_117550) is another VGAM1719 host target gene. LOC203504 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203504 BINDING SITE, designated SEQ ID:43570, to the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57960] Another function of VGAM1719 is therefore inhibition of LOC203504 (Accession XM\_117550). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203504. LOC256682 (Accession XM\_174473) is another VGAM1719 host target gene. LOC256682 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256682 BINDING SITE, designated SEQ ID:46593, to

the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57961] Another function of VGAM1719 is therefore inhibition of LOC256682 (Accession XM\_174473). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256682. LOC257451 (Accession XM\_170960) is another VGAM1719 host target gene. LOC257451 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257451 BINDING SITE, designated SEQ ID:45742, to the nucleotide sequence of VGAM1719 RNA, herein designated VGAM RNA, also designated SEQ ID:4430.

[57962] Another function of VGAM1719 is therefore inhibition of LOC257451 (Accession XM\_170960). Accordingly, utilities of VGAM1719 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257451. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1720 (VGAM1720) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[57963] VGAM1720 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1720 was detected is described hereinabove with reference to Figs. 1–8.

[57964] VGAM1720 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat Cytomegalovirus. VGAM1720 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[57965] VGAM1720 gene encodes a VGAM1720 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1720 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1720 precursor RNA is designated SEQ ID:1706, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1706 is located at position 111844 relative to the genome of Rat Cytomegalovirus.

[57966] VGAM1720 precursor RNA folds onto itself, forming VGAM1720 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[57967] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1720 folded precursor RNA into VGAM1720 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1720 RNA is designated SEQ ID:4431, and is provided hereinbelow with reference to the sequence listing part.

[57968] VGAM1720 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1720 host target RNA, herein designated



VGAM HOST TARGET RNA. VGAM1720 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[57969] VGAM1720 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1720 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1720 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1720 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1720 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[57970] The complementary binding of VGAM1720 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1720 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1720 host target RNA into VGAM1720 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[57971] It is appreciated that VGAM1720 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1720 host target genes. The mRNA of each one of this plurality of VGAM1720 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1720 RNA, herein designated VGAM RNA, and which when bound by VGAM1720 RNA causes inhibition of translation of respective one or more VGAM1720 host target proteins.

[57972] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1720 gene, herein designated VGAM GENE, on one or more VGAM1720 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[57973] It is yet further appreciated that a function of VGAM1720 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of viral infection by Rat Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1720 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1720 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[57974] Nucleotide sequences of the VGAM1720 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1720 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1720 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1720 are further described hereinbelow with reference to Table 1.

[57975] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1720 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1720 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[57976] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1720 gene, herein designated VGAM is inhibition of expression of VGAM1720 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1720 correlate with, and may be deduced from, the identity of the target genes which VGAM1720

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[57977] ACK1 (Accession NM\_005781) is a VGAM1720 host target gene. ACK1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ACK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACK1 BINDING SITE, designated SEQ ID:12360, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57978] A function of VGAM1720 is therefore inhibition of ACK1 (Accession NM\_005781). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACK1. Ankyrin 1, Erythrocytic (ANK1, Accession XM\_016774) is another VGAM1720 host target gene. ANK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ANK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK1 BINDING SITE, designated SEQ ID:30285, to the nucleotide se-

quence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57979] Another function of VGAM1720 is therefore inhibition of Ankyrin 1, Erythrocytic (ANK1, Accession XM\_016774). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK1. Axin 1 (AXIN1, Accession XM\_027520) is another VGAM1720 host target gene. AXIN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AXIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AXIN1 BINDING SITE, designated SEQ ID:30515, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57980] Another function of VGAM1720 is therefore inhibition of Axin 1 (AXIN1, Accession XM\_027520). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AXIN1. AXIN1 Up-regulated 1 (AXUD1, Accession NM\_033027) is another VGAM1720 host target gene.

AXUD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AXUD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AXUD1 BINDING SITE, designated SEQ ID:26920, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57981] Another function of VGAM1720 is therefore inhibition of AXIN1 Up-regulated 1 (AXUD1, Accession NM\_033027). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AXUD1. Bone Morphogenetic Protein 4 (BMP4, Accession NM\_130850) is another VGAM1720 host target gene. BMP4 BINDING SITE1 and BMP4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BMP4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMP4 BINDING SITE1 and BMP4 BINDING SITE2, designated SEQ ID:28387 and SEQ ID:6866 respectively, to the nucleotide

sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57982] Another function of VGAM1720 is therefore inhibition of Bone Morphogenetic Protein 4 (BMP4, Accession NM\_130850), a gene which acts in mesoderm induction, tooth development, limb formation and fracture repair. Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMP4. The function of BMP4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM910. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 2 (DYRK2, Accession NM\_006482) is another VGAM1720 host target gene. DYRK2 BINDING SITE1 and DYRK2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DYRK2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK2 BINDING SITE1 and DYRK2 BINDING SITE2, designated SEQ ID:13209 and SEQ ID:9633 respectively, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM



RNA, also designated SEQ ID:4431.

[57983] Another function of VGAM1720 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 2 (DYRK2, Accession NM\_006482). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK2. E1A Binding Protein P300 (EP300, Accession NM\_001429) is another VGAM1720 host target gene. EP300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EP300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EP300 BINDING SITE, designated SEQ ID:7152, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57984] Another function of VGAM1720 is therefore inhibition of E1A Binding Protein P300 (EP300, Accession NM\_001429), a gene which may have a function in cell cycle regulation. Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EP300. The function of EP300 and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM191. Frizzled Homolog 1 (Drosophila) (FZD1, Accession NM\_003505) is another VGAM1720 host target gene. FZD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FZD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD1 BINDING SITE, designated SEQ ID:9593, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57985] Another function of VGAM1720 is therefore inhibition of Frizzled Homolog 1 (Drosophila) (FZD1, Accession NM\_003505), a gene which may be involved in bone resorption; strongly similar to rat Fzd. Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD1. The function of FZD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM432. UDP-N-acetyl-alpha-D-galactosamine:(N-acety

Ineuraminyl)-galactosylglucosylceramide N-  
 acetylgalactosaminyltransferase (GalNAc-T) (GALGT, Ac-  
 cession NM\_001478) is another VGAM1720 host target  
 gene. GALGT BINDING SITE is HOST TARGET binding site  
 found in the 5` untranslated region of mRNA encoded by  
 GALGT, corresponding to a HOST TARGET binding site  
 such as BINDING SITE I, BINDING SITE II or BINDING SITE III.  
 Table 2 illustrates the complementarity of the nucleotide  
 sequences of GALGT BINDING SITE, designated SEQ  
 ID:7212, to the nucleotide sequence of VGAM1720 RNA,  
 herein designated VGAM RNA, also designated SEQ  
 ID:4431.

[57986] Another function of VGAM1720 is therefore inhibition of  
 UDP-  
 N-  
 acetyl-al-  
 pha-  
 D-galac-  
 tosamine:(N-acetylneuraminyl)-galactosylglucosylceramid  
 e N-acetylgalactosaminyltransferase (GalNAc-T) (GALGT,  
 Accession NM\_001478), a gene which is involved in the  
 biosynthesis of gangliosides gm2, gd2 and ga2. Accord-  
 ingly, utilities of VGAM1720 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with GALGT. The function of GALGT and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM179. Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 6 (KCNA6, Accession NM\_002235) is another VGAM1720 host target gene. KCNA6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNA6 BINDING SITE, designated SEQ ID:8017, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57987] Another function of VGAM1720 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 6 (KCNA6, Accession NM\_002235), a gene which mediates the voltage-dependent potassium ion permeability of excitable membranes. Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with KCNA6. The function of KCNA6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM893. Mannosidase, Alpha, Class 2A, Member 1 (MAN2A1, Accession NM\_002372) is another VGAM1720 host target gene. MAN2A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAN2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN2A1 BINDING SITE, designated SEQ ID:8179, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57988] Another function of VGAM1720 is therefore inhibition of Mannosidase, Alpha, Class 2A, Member 1 (MAN2A1, Accession NM\_002372), a gene which catalyzes the final hydrolytic step in the asparagine-linked oligosaccharide (N-glycan) maturation pathway. Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN2A1. The function of MAN2A1 and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM1410. Protein Kinase, AMP-activated, Beta 1 Non-catalytic Subunit (PRKAB1, Accession NM\_006253) is another VGAM1720 host target gene. PRKAB1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRKAB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAB1 BINDING SITE, designated SEQ ID:12930, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57989] Another function of VGAM1720 is therefore inhibition of Protein Kinase, AMP-activated, Beta 1 Non-catalytic Subunit (PRKAB1, Accession NM\_006253), a gene which is responsible for the regulation of fatty acid synthesis by phosphorylation of acetyl-coa carboxylase. Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAB1. The function of PRKAB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM1384.SORCS2 (Accession NM\_020777) is another VGAM1720 host target gene. SORCS2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SORCS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORCS2 BINDING SITE, designated SEQ ID:21878, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57990] Another function of VGAM1720 is therefore inhibition of SORCS2 (Accession NM\_020777). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORCS2. Zinc Finger Protein 26 (KOX 20) (ZNF26, Accession XM\_053907) is another VGAM1720 host target gene. ZNF26 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF26 BINDING SITE, designated SEQ

ID:36130, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57991] Another function of VGAM1720 is therefore inhibition of Zinc Finger Protein 26 (KOX 20) (ZNF26, Accession XM\_053907), a gene which may be involved in transcriptional regulation. Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF26. The function of ZNF26 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1533.Chromosome 21 Open Reading Frame 93 (C21orf93, Accession NM\_145179) is another VGAM1720 host target gene. C21orf93 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C21orf93, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf93 BINDING SITE, designated SEQ ID:29742, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.



[57992] Another function of VGAM1720 is therefore inhibition of Chromosome 21 Open Reading Frame 93 (C21orf93, Accession NM\_145179). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf93. Caspase Recruitment Domain Family, Member 9 (CARD9, Accession NM\_022352) is another VGAM1720 host target gene. CARD9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARD9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARD9 BINDING SITE, designated SEQ ID:22748, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57993] Another function of VGAM1720 is therefore inhibition of Caspase Recruitment Domain Family, Member 9 (CARD9, Accession NM\_022352). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARD9. CASKIN1 (Accession NM\_020764) is another VGAM1720 host target gene. CASKIN1 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by CASKIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASKIN1 BINDING SITE, designated SEQ ID:21864, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57994] Another function of VGAM1720 is therefore inhibition of CASKIN1 (Accession NM\_020764). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASKIN1. DED (Accession NM\_012138) is another VGAM1720 host target gene. DED BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DED, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DED BINDING SITE, designated SEQ ID:14448, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57995] Another function of VGAM1720 is therefore inhibition of

DED (Accession NM\_012138). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DED. FLJ00001 (Accession XM\_088525) is another VGAM1720 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00001 BINDING SITE, designated SEQ ID:39777, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57996] Another function of VGAM1720 is therefore inhibition of FLJ00001 (Accession XM\_088525). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00001. FLJ12355 (Accession NM\_024988) is another VGAM1720 host target gene. FLJ12355 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12355, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ12355 BINDING SITE, designated SEQ ID:24543, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57997] Another function of VGAM1720 is therefore inhibition of FLJ12355 (Accession NM\_024988). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12355. FLJ12895 (Accession NM\_023926) is another VGAM1720 host target gene. FLJ12895 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12895 BINDING SITE, designated SEQ ID:23405, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57998] Another function of VGAM1720 is therefore inhibition of FLJ12895 (Accession NM\_023926). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12895. FLJ13072 (Accession XM\_117117) is another

VGAM1720 host target gene. FLJ13072 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13072 BINDING SITE, designated SEQ ID:43234, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[57999] Another function of VGAM1720 is therefore inhibition of FLJ13072 (Accession XM\_117117). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13072. FLJ20374 (Accession NM\_017793) is another VGAM1720 host target gene. FLJ20374 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20374, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20374 BINDING SITE, designated SEQ ID:19430, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58000] Another function of VGAM1720 is therefore inhibition of FLJ20374 (Accession NM\_017793). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20374. FLJ20730 (Accession NM\_017945) is another VGAM1720 host target gene. FLJ20730 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20730, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20730 BINDING SITE, designated SEQ ID:19640, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58001] Another function of VGAM1720 is therefore inhibition of FLJ20730 (Accession NM\_017945). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20730. FLJ21596 (Accession NM\_024823) is another VGAM1720 host target gene. FLJ21596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21596 BINDING SITE, designated SEQ ID:24213, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58002] Another function of VGAM1720 is therefore inhibition of FLJ21596 (Accession NM\_024823). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21596. HRIHFB2122 (Accession NM\_007032) is another VGAM1720 host target gene. HRIHFB2122 BINDING SITE1 and HRIHFB2122 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HRIHFB2122, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRIHFB2122 BINDING SITE1 and HRIHFB2122 BINDING SITE2, designated SEQ ID:13901 and SEQ ID:28904 respectively, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58003] Another function of VGAM1720 is therefore inhibition of HRIHFB2122 (Accession NM\_007032). Accordingly, utili-

ties of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRIHFB2122. KIAA0844 (Accession NM\_014951) is another VGAM1720 host target gene. KIAA0844 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0844, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0844 BINDING SITE, designated SEQ ID:17283, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58004] Another function of VGAM1720 is therefore inhibition of KIAA0844 (Accession NM\_014951). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0844. KIAA1319 (Accession NM\_020770) is another VGAM1720 host target gene. KIAA1319 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of



KIAA1319 BINDING SITE, designated SEQ ID:21867, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58005] Another function of VGAM1720 is therefore inhibition of KIAA1319 (Accession NM\_020770). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1319. MGC15437 (Accession NM\_032873) is another VGAM1720 host target gene. MGC15437 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15437 BINDING SITE, designated SEQ ID:26689, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58006] Another function of VGAM1720 is therefore inhibition of MGC15437 (Accession NM\_032873). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15437. MGC2705 (Accession NM\_032701) is another VGAM1720 host target gene. MGC2705 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC2705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2705 BINDING SITE, designated SEQ ID:26417, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58007] Another function of VGAM1720 is therefore inhibition of MGC2705 (Accession NM\_032701). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2705. MOT8 (Accession NM\_018836) is another VGAM1720 host target gene. MOT8 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOT8 BINDING SITE, designated SEQ ID:20824, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58008] Another function of VGAM1720 is therefore inhibition of

MOT8 (Accession NM\_018836). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOT8. Ras and Rab Interactor 3 (RIN3, Accession NM\_024832) is another VGAM1720 host target gene. RIN3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RIN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RIN3 BINDING SITE, designated SEQ ID:24231, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58009] Another function of VGAM1720 is therefore inhibition of Ras and Rab Interactor 3 (RIN3, Accession NM\_024832). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RIN3. RP4-622L5 (Accession NM\_019118) is another VGAM1720 host target gene. RP4-622L5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RP4-622L5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of RP4-622L5 BINDING SITE, designated SEQ ID:21202, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58010] Another function of VGAM1720 is therefore inhibition of RP4-622L5 (Accession NM\_019118). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP4-622L5. Sema Domain, Immunoglobulin Domain (Ig), and GPI Membrane Anchor, (semaphorin) 7A (SEMA7A, Accession NM\_003612) is another VGAM1720 host target gene. SEMA7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA7A BINDING SITE, designated SEQ ID:9664, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58011] Another function of VGAM1720 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), and GPI

Membrane Anchor, (semaphorin) 7A (SEMA7A, Accession NM\_003612). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA7A. Syntaxin 11 (STX11, Accession NM\_003764) is another VGAM1720 host target gene. STX11 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by STX11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STX11 BINDING SITE, designated SEQ ID:9842, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58012] Another function of VGAM1720 is therefore inhibition of Syntaxin 11 (STX11, Accession NM\_003764). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STX11. T2BP (Accession XM\_046111) is another VGAM1720 host target gene. T2BP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by T2BP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of T2BP BINDING SITE, designated SEQ ID:34681, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58013] Another function of VGAM1720 is therefore inhibition of T2BP (Accession XM\_046111). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with T2BP. Three Prime Repair Exonuclease 2 (TREX2, Accession NM\_080699) is another VGAM1720 host target gene. TREX2 BINDING SITE1 and TREX2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TREX2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TREX2 BINDING SITE1 and TREX2 BINDING SITE2, designated SEQ ID:27988 and SEQ ID:14069 respectively, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58014] Another function of VGAM1720 is therefore inhibition of Three Prime Repair Exonuclease 2 (TREX2, Accession

NM\_080699). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TREX2. LOC143666 (Accession XM\_096465) is another VGAM1720 host target gene. LOC143666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143666 BINDING SITE, designated SEQ ID:40370, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58015] Another function of VGAM1720 is therefore inhibition of LOC143666 (Accession XM\_096465). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143666. LOC146138 (Accession XM\_096938) is another VGAM1720 host target gene. LOC146138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC146138 BINDING SITE, designated SEQ ID:40656, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58016] Another function of VGAM1720 is therefore inhibition of LOC146138 (Accession XM\_096938). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146138. LOC148132 (Accession XM\_097408) is another VGAM1720 host target gene. LOC148132 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148132 BINDING SITE, designated SEQ ID:40869, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58017] Another function of VGAM1720 is therefore inhibition of LOC148132 (Accession XM\_097408). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148132. LOC148229 (Accession XM\_086103) is an-



other VGAM1720 host target gene. LOC148229 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148229 BINDING SITE, designated SEQ ID:38496, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58018] Another function of VGAM1720 is therefore inhibition of LOC148229 (Accession XM\_086103). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148229. LOC150935 (Accession XM\_087049) is another VGAM1720 host target gene. LOC150935 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150935 BINDING SITE, designated SEQ ID:39019, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58019] Another function of VGAM1720 is therefore inhibition of LOC150935 (Accession XM\_087049). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150935. LOC151174 (Accession XM\_098013) is another VGAM1720 host target gene. LOC151174 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151174 BINDING SITE, designated SEQ ID:41311, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58020] Another function of VGAM1720 is therefore inhibition of LOC151174 (Accession XM\_098013). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151174. LOC154101 (Accession XM\_094692) is another VGAM1720 host target gene. LOC154101 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154101, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154101 BINDING SITE, designated SEQ ID:40237, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58021] Another function of VGAM1720 is therefore inhibition of LOC154101 (Accession XM\_094692). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154101. LOC202559 (Accession XM\_114504) is another VGAM1720 host target gene. LOC202559 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202559 BINDING SITE, designated SEQ ID:42986, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58022] Another function of VGAM1720 is therefore inhibition of LOC202559 (Accession XM\_114504). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC202559. LOC221876 (Accession XM\_168220) is another VGAM1720 host target gene. LOC221876 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221876 BINDING SITE, designated SEQ ID:45077, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58023] Another function of VGAM1720 is therefore inhibition of LOC221876 (Accession XM\_168220). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221876. LOC253258 (Accession XM\_172870) is another VGAM1720 host target gene. LOC253258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253258 BINDING SITE, designated SEQ ID:46148, to the nucleotide sequence of VGAM1720 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4431.

[58024] Another function of VGAM1720 is therefore inhibition of LOC253258 (Accession XM\_172870). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253258. LOC255146 (Accession XM\_170985) is another VGAM1720 host target gene. LOC255146 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255146 BINDING SITE, designated SEQ ID:45756, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58025] Another function of VGAM1720 is therefore inhibition of LOC255146 (Accession XM\_170985). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255146. LOC257478 (Accession XM\_054745) is another VGAM1720 host target gene. LOC257478 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257478, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257478 BINDING SITE, designated SEQ ID:36183, to the nucleotide sequence of VGAM1720 RNA, herein designated VGAM RNA, also designated SEQ ID:4431.

[58026] Another function of VGAM1720 is therefore inhibition of LOC257478 (Accession XM\_054745). Accordingly, utilities of VGAM1720 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257478. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1721 (VGAM1721) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58027] VGAM1721 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1721 was detected is described hereinabove with reference to Figs. 1-8.

[58028] VGAM1721 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus.

VGAM1721 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58029] VGAM1721 gene encodes a VGAM1721 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1721 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1721 precursor RNA is designated SEQ ID:1707, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1707 is located at position 8494 relative to the genome of Myxoma Virus.

[58030] VGAM1721 precursor RNA folds onto itself, forming VGAM1721 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58031] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1721 folded precursor RNA into VGAM1721 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1721 RNA is designated SEQ ID:4432, and is provided hereinbelow with reference to the sequence listing part.

[58032] VGAM1721 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1721 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1721 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58033] VGAM1721 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1721 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM1721 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1721 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1721 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58034] The complementary binding of VGAM1721 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1721 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1721 host target RNA into VGAM1721 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58035] It is appreciated that VGAM1721 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1721 host target genes. The mRNA of each one of this plurality of VGAM1721 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1721 RNA, herein designated VGAM RNA, and which when bound by VGAM1721 RNA causes inhibition of translation of respective one or more VGAM1721 host target proteins.

[58036] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1721 gene, herein designated VGAM GENE, on one or more VGAM1721 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58037] It is yet further appreciated that a function of VGAM1721 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1721 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM1721 correlate with, and may be deduced from, the identity of the host target genes which VGAM1721 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58038] Nucleotide sequences of the VGAM1721 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1721 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1721 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1721 are further described hereinbelow with reference to Table 1.

[58039] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1721 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1721 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58040] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1721 gene, herein designated VGAM is inhibition of expression of VGAM1721 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1721 correlate with, and may be deduced from, the identity of the target genes which VGAM1721 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58041] G Protein-coupled Receptor 30 (GPR30, Accession NM\_001505) is a VGAM1721 host target gene. GPR30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR30 BINDING SITE, designated SEQ ID:7250, to the

nucleotide sequence of VGAM1721 RNA, herein designated VGAM RNA, also designated SEQ ID:4432.

[58042] A function of VGAM1721 is therefore inhibition of G Protein-coupled Receptor 30 (GPR30, Accession NM\_001505), a gene which receives chemical signals in cell communication in both CNS and peripheral tissues. Accordingly, utilities of VGAM1721 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR30. The function of GPR30 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM171.FLJ12788 (Accession NM\_022492) is another VGAM1721 host target gene. FLJ12788 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12788, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12788 BINDING SITE, designated SEQ ID:22873, to the nucleotide sequence of VGAM1721 RNA, herein designated VGAM RNA, also designated SEQ ID:4432.

[58043] Another function of VGAM1721 is therefore inhibition of

FLJ12788 (Accession NM\_022492). Accordingly, utilities of VGAM1721 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12788. HGC6.1.1 (Accession NM\_014354) is another VGAM1721 host target gene. HGC6.1.1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGC6.1.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGC6.1.1 BINDING SITE, designated SEQ ID:15684, to the nucleotide sequence of VGAM1721 RNA, herein designated VGAM RNA, also designated SEQ ID:4432.

[58044] Another function of VGAM1721 is therefore inhibition of HGC6.1.1 (Accession NM\_014354). Accordingly, utilities of VGAM1721 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGC6.1.1. LOC254423 (Accession XM\_173286) is another VGAM1721 host target gene. LOC254423 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC254423 BINDING SITE, designated SEQ ID:46529, to the nucleotide sequence of VGAM1721 RNA, herein designated VGAM RNA, also designated SEQ ID:4432.

[58045] Another function of VGAM1721 is therefore inhibition of LOC254423 (Accession XM\_173286). Accordingly, utilities of VGAM1721 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254423. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1722 (VGAM1722) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58046] VGAM1722 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1722 was detected is described hereinabove with reference to Figs. 1–8.

[58047] VGAM1722 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus. VGAM1722 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[58048] VGAM1722 gene encodes a VGAM1722 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1722 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1722 precursor RNA is designated SEQ ID:1708, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1708 is located at position 4765 relative to the genome of Myxoma Virus.

[58049] VGAM1722 precursor RNA folds onto itself, forming VGAM1722 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58050] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1722 folded precursor RNA into VGAM1722 RNA, herein designated VGAM RNA, a single stranded ~22



nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1722 RNA is designated SEQ ID:4433, and is provided hereinbelow with reference to the sequence listing part.

[58051] VGAM1722 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1722 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1722 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58052] VGAM1722 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1722 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1722 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1722 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1722 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58053] The complementary binding of VGAM1722 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1722 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1722 host target RNA into VGAM1722 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58054] It is appreciated that VGAM1722 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1722 host target genes. The mRNA of each one of this plurality of VGAM1722 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1722 RNA, herein designated VGAM RNA, and which when bound by VGAM1722 RNA causes inhibition of translation of respective one or more VGAM1722 host target proteins.

[58055] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1722 gene, herein designated VGAM GENE, on one or more VGAM1722 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58056] It is yet further appreciated that a function of VGAM1722 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM1722 correlate with, and may be deduced from, the identity of the host target genes which VGAM1722 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58057] Nucleotide sequences of the VGAM1722 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1722 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1722 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1722 are further described hereinbelow with reference to Table 1.

[58058] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1722 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1722 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58059] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1722 gene, herein designated VGAM is inhibition of expression of VGAM1722 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1722 correlate with, and may be deduced from, the identity of the target genes which VGAM1722 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58060] Coronin, Actin Binding Protein, 2B (CORO2B, Accession XM\_035403) is a VGAM1722 host target gene. CORO2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CORO2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CORO2B BINDING SITE, designated SEQ ID:32253, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ

ID:4433.

[58061] A function of VGAM1722 is therefore inhibition of Coro-  
nin, Actin Binding Protein, 2B (CORO2B, Accession  
XM\_035403), a gene which may play a role in the reorga-  
nization of neuronal actin structure. Accordingly, utilities  
of VGAM1722 include diagnosis, prevention and treat-  
ment of diseases and clinical conditions associated with  
CORO2B. The function of CORO2B and its association with  
various diseases and clinical conditions, has been estab-  
lished by previous studies, as described hereinabove with  
reference to VGAM923. Forkhead Box E3 (FOX E3, Acces-  
sion NM\_012186) is another VGAM1722 host target gene.  
FOX E3 BINDING SITE1 and FOX E3 BINDING SITE2 are HOST  
TARGET binding sites found in untranslated regions of  
mRNA encoded by FOX E3, corresponding to HOST TARGET  
binding sites such as BINDING SITE I, BINDING SITE II or  
BINDING SITE III. Table 2 illustrates the complementarity  
of the nucleotide sequences of FOX E3 BINDING SITE1 and  
FOX E3 BINDING SITE2, designated SEQ ID:14471 and SEQ  
ID:14468 respectively, to the nucleotide sequence of  
VGAM1722 RNA, herein designated VGAM RNA, also des-  
ignated SEQ ID:4433.

[58062] Another function of VGAM1722 is therefore inhibition of

Forkhead Box E3 (FOXE3, Accession NM\_012186), a gene which regulates embryonic development. Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXE3. The function of FOXE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM632.FLJ22002 (Accession NM\_024838) is another VGAM1722 host target gene. FLJ22002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22002 BINDING SITE, designated SEQ ID:24247, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58063] Another function of VGAM1722 is therefore inhibition of FLJ22002 (Accession NM\_024838). Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22002. Fucosyltransferase 10 (alpha (1,3) Fucosyl-

transferase) (FUT10, Accession NM\_032664) is another VGAM1722 host target gene. FUT10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT10 BINDING SITE, designated SEQ ID:26392, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58064] Another function of VGAM1722 is therefore inhibition of Fucosyltransferase 10 (alpha (1,3) Fucosyltransferase) (FUT10, Accession NM\_032664). Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT10. KIAA0014 (Accession NM\_014665) is another VGAM1722 host target gene. KIAA0014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0014 BINDING SITE, designated SEQ ID:16120, to the nucleotide sequence of



VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58065] Another function of VGAM1722 is therefore inhibition of KIAA0014 (Accession NM\_014665). Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0014. KIAA0794 (Accession XM\_087353) is another VGAM1722 host target gene. KIAA0794 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0794 BINDING SITE, designated SEQ ID:39178, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58066] Another function of VGAM1722 is therefore inhibition of KIAA0794 (Accession XM\_087353). Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0794. MIL1 (Accession NM\_015367) is another VGAM1722 host target gene. MIL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by MIL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIL1 BINDING SITE, designated SEQ ID:17667, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58067] Another function of VGAM1722 is therefore inhibition of MIL1 (Accession NM\_015367). Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIL1. Prefoldin 1 (PFDN1, Accession NM\_002622) is another VGAM1722 host target gene. PFDN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PFDN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PFDN1 BINDING SITE, designated SEQ ID:8482, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58068] Another function of VGAM1722 is therefore inhibition of Prefoldin 1 (PFDN1, Accession NM\_002622). Accordingly,

utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PFDN1. LOC145195 (Accession XM\_096731) is another VGAM1722 host target gene. LOC145195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145195 BINDING SITE, designated SEQ ID:40516, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58069] Another function of VGAM1722 is therefore inhibition of LOC145195 (Accession XM\_096731). Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145195. LOC157697 (Accession XM\_088365) is another VGAM1722 host target gene. LOC157697 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157697, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC157697 BINDING SITE, designated SEQ ID:39646, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58070] Another function of VGAM1722 is therefore inhibition of LOC157697 (Accession XM\_088365). Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157697. LOC222160 (Accession XM\_168431) is another VGAM1722 host target gene. LOC222160 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222160 BINDING SITE, designated SEQ ID:45165, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58071] Another function of VGAM1722 is therefore inhibition of LOC222160 (Accession XM\_168431). Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222160. LOC257449 (Accession XM\_031562) is another VGAM1722 host target gene. LOC257449 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257449 BINDING SITE, designated SEQ ID:31426, to the nucleotide sequence of VGAM1722 RNA, herein designated VGAM RNA, also designated SEQ ID:4433.

[58072] Another function of VGAM1722 is therefore inhibition of LOC257449 (Accession XM\_031562). Accordingly, utilities of VGAM1722 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257449. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1723 (VGAM1723) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58073] VGAM1723 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1723 was detected is described hereinabove with reference to Figs. 1-8.

[58074] VGAM1723 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus.

VGAM1723 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58075] VGAM1723 gene encodes a VGAM1723 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1723 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1723 precursor RNA is designated SEQ ID:1709, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1709 is located at position 4097 relative to the genome of Myxoma Virus.

[58076] VGAM1723 precursor RNA folds onto itself, forming VGAM1723 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[58077] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1723 folded precursor RNA into VGAM1723 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1723 RNA is designated SEQ ID:4434, and is provided hereinbelow with reference to the sequence listing part.

[58078] VGAM1723 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1723 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1723 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58079] VGAM1723 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1723 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1723 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1723 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1723 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[58080] The complementary binding of VGAM1723 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1723 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE



II and BINDING SITE III, inhibits translation of VGAM1723 host target RNA into VGAM1723 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58081] It is appreciated that VGAM1723 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1723 host target genes. The mRNA of each one of this plurality of VGAM1723 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1723 RNA, herein designated VGAM RNA, and which when bound by VGAM1723 RNA causes inhibition of translation of respective one or more VGAM1723 host target proteins.

[58082] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1723 gene, herein designated VGAM GENE, on one or more VGAM1723 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58083] It is yet further appreciated that a function of VGAM1723 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1723 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM1723 correlate with, and may be deduced from, the identity of the host target genes which VGAM1723 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58084] Nucleotide sequences of the VGAM1723 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1723 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1723 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1723 are further described hereinbelow with reference to Table 1.

[58085] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1723 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1723 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58086] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1723 gene, herein designated VGAM is inhibition of expression of VGAM1723 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1723 correlate with, and may be deduced from, the identity of the target genes which VGAM1723 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58087] LOC122210 (Accession XM\_058609) is a VGAM1723 host target gene. LOC122210 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC122210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LOC122210 BINDING SITE, designated SEQ ID:36681, to the nucleotide sequence of VGAM1723 RNA, herein designated VGAM RNA, also designated SEQ ID:4434.

[58088] A function of VGAM1723 is therefore inhibition of LOC122210 (Accession XM\_058609). Accordingly, utilities of VGAM1723 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122210. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1724 (VGAM1724) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58089] VGAM1724 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1724 was detected is described hereinabove with reference to Figs. 1–8.

[58090] VGAM1724 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabies Virus. VGAM1724 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58091] VGAM1724 gene encodes a VGAM1724 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1724 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1724 precursor RNA is designated SEQ ID:1710, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1710 is located at position 3898 relative to the genome of Rabies Virus.

[58092] VGAM1724 precursor RNA folds onto itself, forming VGAM1724 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58093] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1724 folded precursor RNA into VGAM1724 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1724 RNA is designated SEQ ID:4435, and is provided hereinbelow with reference to the sequence listing part.

[58094] VGAM1724 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1724 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1724 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58095] VGAM1724 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1724 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1724 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1724 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1724 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58096] The complementary binding of VGAM1724 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1724 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1724 host target RNA into VGAM1724 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58097] It is appreciated that VGAM1724 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1724 host target genes. The mRNA of each one of this plurality of VGAM1724 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1724 RNA, herein designated VGAM RNA, and which when bound by VGAM1724 RNA causes inhibition of translation of respective one or more VGAM1724 host target proteins.

[58098] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1724 gene, herein designated VGAM GENE, on one or more VGAM1724 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these



other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[58099] It is yet further appreciated that a function of VGAM1724 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1724 include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGAM1724 correlate with, and may be deduced from, the identity of the host target genes which VGAM1724 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58100] Nucleotide sequences of the VGAM1724 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1724 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1724 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1724 are further described hereinbelow with reference to Table 1.

[58101] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1724 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1724 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[58102] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1724 gene, herein designated VGAM is inhibition of expression of VGAM1724 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1724 correlate with, and may be deduced from, the identity of the target genes which VGAM1724 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58103] Synaptogyrin 3 (SYNGR3, Accession NM\_004209) is a VGAM1724 host target gene. SYNGR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNGR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNGR3 BINDING SITE, designated SEQ ID:10406, to the nucleotide sequence of VGAM1724 RNA, herein designated VGAM RNA, also designated SEQ ID:4435.

[58104] A function of VGAM1724 is therefore inhibition of Synaptogyrin 3 (SYNGR3, Accession NM\_004209). Accordingly, utilities of VGAM1724 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with SYNGR3. HSPC195 (Accession XM\_087785) is another VGAM1724 host target gene. HSPC195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC195 BINDING SITE, designated SEQ ID:39420, to the nucleotide sequence of VGAM1724 RNA, herein designated VGAM RNA, also designated SEQ ID:4435.

[58105] Another function of VGAM1724 is therefore inhibition of HSPC195 (Accession XM\_087785). Accordingly, utilities of VGAM1724 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC195. KIAA1677 (Accession XM\_040383) is another VGAM1724 host target gene. KIAA1677 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1677, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1677 BINDING SITE, designated SEQ ID:33290, to the nucleotide sequence of VGAM1724 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4435.

[58106] Another function of VGAM1724 is therefore inhibition of KIAA1677 (Accession XM\_040383). Accordingly, utilities of VGAM1724 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1677. LOC221042 (Accession XM\_167669) is another VGAM1724 host target gene. LOC221042 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221042 BINDING SITE, designated SEQ ID:44759, to the nucleotide sequence of VGAM1724 RNA, herein designated VGAM RNA, also designated SEQ ID:4435.

[58107] Another function of VGAM1724 is therefore inhibition of LOC221042 (Accession XM\_167669). Accordingly, utilities of VGAM1724 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221042. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1725 (VGAM1725) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58108] VGAM1725 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1725 was detected is described hereinabove with reference to Figs. 1–8.

[58109] VGAM1725 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabies Virus. VGAM1725 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58110] VGAM1725 gene encodes a VGAM1725 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1725 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1725 precursor RNA is designated SEQ ID:1711, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1711 is located at position 8659 relative to the genome of Rabies Virus.

[58111] VGAM1725 precursor RNA folds onto itself, forming VGAM1725 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58112] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1725 folded precursor RNA into VGAM1725 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1725 RNA is designated SEQ ID:4436, and is provided hereinbelow with reference to the sequence listing part.

[58113] VGAM1725 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1725 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1725 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58114] VGAM1725 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1725 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1725 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1725 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1725 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in



the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58115] The complementary binding of VGAM1725 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1725 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1725 host target RNA into VGAM1725 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58116] It is appreciated that VGAM1725 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1725 host target genes. The mRNA of each one of this plurality of VGAM1725 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1725 RNA, herein designated VGAM RNA, and which when bound by VGAM1725 RNA causes inhibition of translation of respective one or more VGAM1725 host target proteins.

[58117] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1725 gene, herein designated VGAM GENE, on one or more VGAM1725 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58118] It is yet further appreciated that a function of VGAM1725 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1725 include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGAM1725 correlate with, and may be deduced from, the identity of the host target genes which VGAM1725 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[58119] Nucleotide sequences of the VGAM1725 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1725 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1725 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1725 are further described hereinbelow with reference to Table 1.

[58120] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1725 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1725 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58121] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1725 gene, herein designated VGAM is inhibition of expression of VGAM1725 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1725 correlate with, and may be deduced from, the identity of the target genes which VGAM1725 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58122] ADP-ribosylation Factor 3 (ARF3, Accession NM\_001659) is a VGAM1725 host target gene. ARF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARF3 BINDING SITE, designated SEQ ID:7378, to the nucleotide sequence of VGAM1725 RNA, herein designated VGAM RNA, also designated SEQ ID:4436.

[58123] A function of VGAM1725 is therefore inhibition of ADP-ribosylation Factor 3 (ARF3, Accession NM\_001659). Accordingly, utilities of VGAM1725 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARF3. Platelet-activating Factor Acetylhydrolase, Isoform Ib, Alpha Subunit 45kDa (PAFAH1B1, Accession NM\_000430) is another VGAM1725 host target gene. PAFAH1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAFAH1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAFAH1B1 BINDING SITE, desig-

nated SEQ ID:6008, to the nucleotide sequence of VGAM1725 RNA, herein designated VGAM RNA, also designated SEQ ID:4436.

[58124] Another function of VGAM1725 is therefore inhibition of Platelet-activating Factor Acetylhydrolase, Isoform Ib, Alpha Subunit 45kDa (PAFAH1B1, Accession NM\_000430). Accordingly, utilities of VGAM1725 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAFAH1B1. FLJ10697 (Accession NM\_018181) is another VGAM1725 host target gene. FLJ10697 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10697, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10697 BINDING SITE, designated SEQ ID:20014, to the nucleotide sequence of VGAM1725 RNA, herein designated VGAM RNA, also designated SEQ ID:4436.

[58125] Another function of VGAM1725 is therefore inhibition of FLJ10697 (Accession NM\_018181). Accordingly, utilities of VGAM1725 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10697. FLJ22679 (Accession NM\_032227) is another VGAM1725 host target gene. FLJ22679 BINDING SITE1 and FLJ22679 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ22679, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22679 BINDING SITE1 and FLJ22679 BINDING SITE2, designated SEQ ID:25953 and SEQ ID:19266 respectively, to the nucleotide sequence of VGAM1725 RNA, herein designated VGAM RNA, also designated SEQ ID:4436.

[58126] Another function of VGAM1725 is therefore inhibition of FLJ22679 (Accession NM\_032227). Accordingly, utilities of VGAM1725 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22679. Suppression of Tumorigenicity 7 Like (ST7L, Accession NM\_138727) is another VGAM1725 host target gene. ST7L BINDING SITE1 through ST7L BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ST7L, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the comple-

mentarity of the nucleotide sequences of ST7L BINDING SITE1 through ST7L BINDING SITE3, designated SEQ ID:28977, SEQ ID:19335 and SEQ ID:29207 respectively, to the nucleotide sequence of VGAM1725 RNA, herein designated VGAM RNA, also designated SEQ ID:4436.

[58127] Another function of VGAM1725 is therefore inhibition of Suppression of Tumorigenicity 7 Like (ST7L, Accession NM\_138727). Accordingly, utilities of VGAM1725 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST7L. LOC116028 (Accession XM\_057225) is another VGAM1725 host target gene. LOC116028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116028 BINDING SITE, designated SEQ ID:36492, to the nucleotide sequence of VGAM1725 RNA, herein designated VGAM RNA, also designated SEQ ID:4436.

[58128] Another function of VGAM1725 is therefore inhibition of LOC116028 (Accession XM\_057225). Accordingly, utilities of VGAM1725 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC116028. LOC150236 (Accession XM\_086824) is another VGAM1725 host target gene. LOC150236 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150236 BINDING SITE, designated SEQ ID:38906, to the nucleotide sequence of VGAM1725 RNA, herein designated VGAM RNA, also designated SEQ ID:4436.

[58129] Another function of VGAM1725 is therefore inhibition of LOC150236 (Accession XM\_086824). Accordingly, utilities of VGAM1725 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150236. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1726 (VGAM1726) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58130] VGAM1726 is a novel bioinformatically detected regula-



tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1726 was detected is described hereinabove with reference to Figs. 1–8.

[58131] VGAM1726 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabies Virus. VGAM1726 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58132] VGAM1726 gene encodes a VGAM1726 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1726 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1726 precursor RNA is designated SEQ ID:1712, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1712 is located at position 9658 relative to the genome of Rabies Virus.

[58133] VGAM1726 precursor RNA folds onto itself, forming VGAM1726 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58134] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1726 folded precursor RNA into VGAM1726 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1726 RNA is designated SEQ ID:4437, and is provided hereinbelow with reference to the sequence listing part.

[58135] VGAM1726 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1726 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1726 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58136] VGAM1726 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1726 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1726 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1726 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1726 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[58137] The complementary binding of VGAM1726 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1726 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1726 host target RNA into VGAM1726 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58138] It is appreciated that VGAM1726 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1726 host target genes. The mRNA of each one of this plurality of VGAM1726 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1726 RNA, herein designated VGAM RNA, and which when bound by VGAM1726 RNA causes inhibition of translation of respective one or more VGAM1726 host target proteins.

[58139] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1726 gene, herein designated VGAM GENE, on one or more VGAM1726 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58140] It is yet further appreciated that a function of VGAM1726 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1726 include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGAM1726 correlate with, and may be deduced from, the identity of the host target genes which VGAM1726 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58141] Nucleotide sequences of the VGAM1726 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1726 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1726 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1726 are further described hereinbelow with reference to Table 1.

[58142] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1726 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1726 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58143] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1726 gene, herein designated VGAM is inhibition of expression of VGAM1726 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1726 correlate with, and may be deduced from, the identity of the target genes which VGAM1726 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58144] G Protein-coupled Receptor, Family C, Group 5, Member B (GPRC5B, Accession NM\_016235) is a VGAM1726 host target gene. GPRC5B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by GPRC5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPRC5B BINDING SITE, designated SEQ ID:18351, to the nucleotide sequence of VGAM1726 RNA, herein designated VGAM RNA, also designated SEQ ID:4437.

[58145] A function of VGAM1726 is therefore inhibition of G Protein-coupled Receptor, Family C, Group 5, Member B (GPRC5B, Accession NM\_016235), a gene which belongs to G protein-coupled receptor. Accordingly, utilities of VGAM1726 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPRC5B. The function of GPRC5B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM131.KIAA0893 (Accession NM\_014969) is another VGAM1726 host target gene. KIAA0893 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0893 BINDING SITE, designated SEQ ID:17361, to the nucleotide sequence of VGAM1726 RNA, herein designated VGAM RNA, also designated SEQ ID:4437.

[58146] Another function of VGAM1726 is therefore inhibition of KIAA0893 (Accession NM\_014969). Accordingly, utilities of VGAM1726 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0893. KIAA1596 (Accession XM\_048128) is another VGAM1726 host target gene. KIAA1596 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1596 BINDING SITE, designated SEQ ID:35118, to the nucleotide sequence of VGAM1726 RNA, herein designated VGAM RNA, also designated SEQ ID:4437.

[58147] Another function of VGAM1726 is therefore inhibition of KIAA1596 (Accession XM\_048128). Accordingly, utilities of VGAM1726 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1596. MGC14836 (Accession NM\_033412) is another VGAM1726 host target gene. MGC14836 BINDING SITE is



HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC14836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14836 BINDING SITE, designated SEQ ID:27236, to the nucleotide sequence of VGAM1726 RNA, herein designated VGAM RNA, also designated SEQ ID:4437.

[58148] Another function of VGAM1726 is therefore inhibition of MGC14836 (Accession NM\_033412). Accordingly, utilities of VGAM1726 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14836. PRSC (Accession NM\_006587) is another VGAM1726 host target gene. PRSC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRSC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRSC BINDING SITE, designated SEQ ID:13348, to the nucleotide sequence of VGAM1726 RNA, herein designated VGAM RNA, also designated SEQ ID:4437.

[58149] Another function of VGAM1726 is therefore inhibition of

PRSC (Accession NM\_006587). Accordingly, utilities of VGAM1726 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRSC. LOC152627 (Accession XM\_087495) is another VGAM1726 host target gene. LOC152627 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152627 BINDING SITE, designated SEQ ID:39297, to the nucleotide sequence of VGAM1726 RNA, herein designated VGAM RNA, also designated SEQ ID:4437.

[58150] Another function of VGAM1726 is therefore inhibition of LOC152627 (Accession XM\_087495). Accordingly, utilities of VGAM1726 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152627. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1727 (VGAM1727) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[58151] VGAM1727 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1727 was detected is described hereinabove with reference to Figs. 1–8.

[58152] VGAM1727 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabies Virus. VGAM1727 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58153] VGAM1727 gene encodes a VGAM1727 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1727 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1727 precursor RNA is designated SEQ ID:1713, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1713 is located at position 8962 relative to the genome of Rabies Virus.

[58154] VGAM1727 precursor RNA folds onto itself, forming VGAM1727 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58155] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1727 folded precursor RNA into VGAM1727 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1727 RNA is designated SEQ ID:4438, and is provided hereinbelow with reference to the sequence listing part.

[58156] VGAM1727 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1727 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1727 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[58157] VGAM1727 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1727 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1727 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1727 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1727 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58158] The complementary binding of VGAM1727 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1727 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1727 host target RNA into VGAM1727 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58159] It is appreciated that VGAM1727 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1727 host target genes. The mRNA of each one of this plurality of VGAM1727 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1727 RNA, herein designated VGAM RNA, and which when bound by VGAM1727 RNA causes inhibition of translation of respective one or more VGAM1727 host target proteins.

[58160] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1727 gene, herein designated VGAM GENE, on one or more VGAM1727 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58161] It is yet further appreciated that a function of VGAM1727 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1727 include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGAM1727 correlate with, and may be deduced from, the identity of the host target genes which VGAM1727 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58162] Nucleotide sequences of the VGAM1727 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1727 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1727 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1727 are further  
described hereinbelow with reference to Table 1.

[58163] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1727 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1727 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[58164] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1727 gene, herein designated VGAM is  
inhibition of expression of VGAM1727 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1727 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1727  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[58165] Ankyrin-like with Transmembrane Domains 1 (ANKTM1,  
Accession NM\_007332) is a VGAM1727 host target gene.



ANKTM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKTM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKTM1 BINDING SITE, designated SEQ ID:14256, to the nucleotide sequence of VGAM1727 RNA, herein designated VGAM RNA, also designated SEQ ID:4438.

[58166] A function of VGAM1727 is therefore inhibition of Ankyrin-like with Transmembrane Domains 1 (ANKTM1, Accession NM\_007332), a gene which attaches integral membrane proteins to cytoskeletal elements. Accordingly, utilities of VGAM1727 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKTM1. The function of ANKTM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM644. Chitinase 3-like 1 (cartilage glycoprotein-39) (CHI3L1, Accession NM\_001276) is another VGAM1727 host target gene. CHI3L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHI3L1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHI3L1 BINDING SITE, designated SEQ ID:6941, to the nucleotide sequence of VGAM1727 RNA, herein designated VGAM RNA, also designated SEQ ID:4438.

[58167] Another function of VGAM1727 is therefore inhibition of Chitinase 3-like 1 (cartilage glycoprotein-39) (CHI3L1, Accession NM\_001276), a gene which participates in the capacity of cells to respond to and cope with changes. Accordingly, utilities of VGAM1727 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHI3L1. The function of CHI3L1 has been established by previous studies. The major function of articular chondrocytes in growing and maturing cartilage is the deposition and remodeling of the cartilage matrix. In adult cartilage, the matrix must be maintained rather than formed. Chondrocytes secrete a variety of proteins. One of the major secreted proteins of human articular chondrocytes in monolayer or explant culture is referred to as human cartilage glycoprotein-39 (HC gp-39). HC gp-39 is also known as YKL-40. The name 'YKL' refers to the sequence of the amino terminus of the protein. (See also

YKL-39, 601526.) Hakala et al. (1993) purified HC gp-39 and determined the sequence of the cDNA. The protein is predicted to contain 383 amino acids, and has regions of similarity to several bacterial and fungal chitinases. HC gp-39 protein did not, however, possess any detectable chitinolytic activity. Hakala et al. (1993) found that expression of the GP39 gene by Northern blotting and RT-PCR was not restricted to chondrocytes. GP39 mRNA was detected in liver and human articular chondrocytes. Neither GP39 protein nor GP39 mRNA was detectable in normal newborn or adult human articular cartilage, but the mRNA was detected in cartilage obtained from patients with rheumatoid arthritis or at autopsy. By genomic sequence analysis, Rehli et al. (1997) determined that the CHI3L1 gene contains 10 exons and spans 8 kb. Primer extension and S1 nuclease protection analyses of the proximal promoter region identified transcriptional initiation sites 82 and 126 nucleotides upstream of the start codon.

[58168] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58169] Hakala, B. E.; White, C.; Recklies, A. D. : Human cartilage

gp-39, a major secretory product of articular chondrocytes and synovial cells, is a mammalian member of a chitinase protein family. J. Biol. Chem. 268: 25803-25810, 1993. ; and

[58170] Rehli, M.; Krause, S. W.; Andreesen, R. : Molecular characterization of the gene for human cartilage gp-39 (CHI3L1), a member of the chitinase protein family and marker for late stages.

[58171] Further studies establishing the function and utilities of CHI3L1 are found in John Hopkins OMIM database record ID 601525, and in cited publications numbered 6533-6534 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nuclear Receptor Subfamily 2, Group E, Member 1 (NR2E1, Accession NM\_003269) is another VGAM1727 host target gene. NR2E1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NR2E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR2E1 BINDING SITE, designated SEQ ID:9278, to the nucleotide sequence of VGAM1727 RNA, herein designated VGAM RNA, also designated SEQ ID:4438.

[58172] Another function of VGAM1727 is therefore inhibition of Nuclear Receptor Subfamily 2, Group E, Member 1 (NR2E1, Accession NM\_003269), a gene which may be required for brain development and be involved in the regulation of retinal development . Accordingly, utilities of VGAM1727 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR2E1. The function of NR2E1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM689.FLJ10392 (Accession NM\_018084) is another VGAM1727 host target gene. FLJ10392 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10392, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10392 BINDING SITE, designated SEQ ID:19847, to the nucleotide sequence of VGAM1727 RNA, herein designated VGAM RNA, also designated SEQ ID:4438.

[58173] Another function of VGAM1727 is therefore inhibition of FLJ10392 (Accession NM\_018084). Accordingly, utilities of VGAM1727 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ10392. FLJ23511 (Accession NM\_032239) is another VGAM1727 host target gene. FLJ23511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23511 BINDING SITE, designated SEQ ID:25963, to the nucleotide sequence of VGAM1727 RNA, herein designated VGAM RNA, also designated SEQ ID:4438.

[58174] Another function of VGAM1727 is therefore inhibition of FLJ23511 (Accession NM\_032239). Accordingly, utilities of VGAM1727 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23511. KIAA0527 (Accession XM\_171054) is another VGAM1727 host target gene. KIAA0527 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0527 BINDING SITE, designated SEQ ID:45847, to the

nucleotide sequence of VGAM1727 RNA, herein designated VGAM RNA, also designated SEQ ID:4438.

[58175] Another function of VGAM1727 is therefore inhibition of KIAA0527 (Accession XM\_171054). Accordingly, utilities of VGAM1727 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0527. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1728 (VGAM1728) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58176] VGAM1728 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1728 was detected is described hereinabove with reference to Figs. 1–8.

[58177] VGAM1728 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabies Virus. VGAM1728 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58178] VGAM1728 gene encodes a VGAM1728 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1728 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1728 precursor RNA is designated SEQ ID:1714, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1714 is located at position 4718 relative to the genome of Rabies Virus.

- [58179] VGAM1728 precursor RNA folds onto itself, forming VGAM1728 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [58180] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1728 folded precursor RNA into VGAM1728 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1728 RNA is designated SEQ ID:4439, and is provided hereinbelow with reference to the sequence listing part.

[58181] VGAM1728 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1728 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1728 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58182] VGAM1728 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1728 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1728 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1728 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1728 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58183] The complementary binding of VGAM1728 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1728 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1728 host target RNA into VGAM1728 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58184] It is appreciated that VGAM1728 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1728 host target genes. The mRNA of

each one of this plurality of VGAM1728 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1728 RNA, herein designated VGAM RNA, and which when bound by VGAM1728 RNA causes inhibition of translation of respective one or more VGAM1728 host target proteins.

[58185] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1728 gene, herein designated VGAM GENE, on one or more VGAM1728 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[58186] It is yet further appreciated that a function of VGAM1728 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1728 include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGAM1728 correlate with, and may be deduced from, the identity of the host target genes which VGAM1728 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58187] Nucleotide sequences of the VGAM1728 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1728 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1728 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1728 are further described hereinbelow with reference to Table 1.

[58188] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1728 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1728 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58189] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1728 gene, herein designated VGAM is inhibition of expression of VGAM1728 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1728 correlate with, and may be deduced from, the identity of the target genes which VGAM1728 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58190] ATPase, H<sup>+</sup> Transporting, Lysosomal 13kDa, V1 Subunit G Isoform 2 (ATP6V1G2, Accession NM\_130463) is a VGAM1728 host target gene. ATP6V1G2 BINDING SITE1 and ATP6V1G2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ATP6V1G2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP6V1G2 BINDING SITE1 and ATP6V1G2 BINDING SITE2, designated SEQ ID:28223 and SEQ ID:28697 respectively, to the nucleotide sequence of VGAM1728 RNA, herein designated VGAM RNA, also designated SEQ ID:4439.

[58191] A function of VGAM1728 is therefore inhibition of ATPase, H<sup>+</sup> Transporting, Lysosomal 13kDa, V1 Subunit G Isoform 2 (ATP6V1G2, Accession NM\_130463). Accordingly, utilities of VGAM1728 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP6V1G2. FLJ11806 (Accession NM\_024824) is another VGAM1728 host target gene. FLJ11806 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11806, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11806 BINDING SITE, designated SEQ ID:24215, to the nucleotide sequence of VGAM1728 RNA, herein designated VGAM RNA, also designated SEQ ID:4439.

[58192] Another function of VGAM1728 is therefore inhibition of FLJ11806 (Accession NM\_024824). Accordingly, utilities of VGAM1728 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11806. FLJ22055 (Accession NM\_024779) is another VGAM1728 host target gene. FLJ22055 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22055, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22055 BINDING SITE, designated SEQ ID:24146, to the nucleotide sequence of VGAM1728 RNA, herein designated VGAM RNA, also designated SEQ ID:4439.

[58193] Another function of VGAM1728 is therefore inhibition of FLJ22055 (Accession NM\_024779). Accordingly, utilities of VGAM1728 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22055. KIAA0960 (Accession XM\_166543) is another VGAM1728 host target gene. KIAA0960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0960 BINDING SITE, designated SEQ ID:44515, to the nucleotide sequence of VGAM1728 RNA, herein designated VGAM RNA, also designated SEQ ID:4439.

[58194] Another function of VGAM1728 is therefore inhibition of KIAA0960 (Accession XM\_166543). Accordingly, utilities of VGAM1728 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0960. KIAA1922 (Accession XM\_057040) is another VGAM1728 host target gene. KIAA1922 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1922 BINDING SITE, designated SEQ ID:36461, to the nucleotide sequence of VGAM1728 RNA, herein designated VGAM RNA, also designated SEQ ID:4439.

[58195] Another function of VGAM1728 is therefore inhibition of KIAA1922 (Accession XM\_057040). Accordingly, utilities of VGAM1728 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1922. MIC2 Like 1 (MIC2L1, Accession NM\_031462) is another VGAM1728 host target gene. MIC2L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MIC2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIC2L1 BINDING SITE, designated SEQ ID:25492, to the



nucleotide sequence of VGAM1728 RNA, herein designated VGAM RNA, also designated SEQ ID:4439.

[58196] Another function of VGAM1728 is therefore inhibition of MIC2 Like 1 (MIC2L1, Accession NM\_031462). Accordingly, utilities of VGAM1728 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIC2L1. PXR2b (Accession NM\_016559) is another VGAM1728 host target gene. PXR2b BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PXR2b, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PXR2b BINDING SITE, designated SEQ ID:18634, to the nucleotide sequence of VGAM1728 RNA, herein designated VGAM RNA, also designated SEQ ID:4439.

[58197] Another function of VGAM1728 is therefore inhibition of PXR2b (Accession NM\_016559). Accordingly, utilities of VGAM1728 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PXR2b. LOC206426 (Accession XM\_116505) is another VGAM1728 host target gene. LOC206426 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC206426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC206426 BINDING SITE, designated SEQ ID:43116, to the nucleotide sequence of VGAM1728 RNA, herein designated VGAM RNA, also designated SEQ ID:4439.

[58198] Another function of VGAM1728 is therefore inhibition of LOC206426 (Accession XM\_116505). Accordingly, utilities of VGAM1728 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC206426. LOC92935 (Accession XM\_048197) is another VGAM1728 host target gene. LOC92935 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92935 BINDING SITE, designated SEQ ID:35130, to the nucleotide sequence of VGAM1728 RNA, herein designated VGAM RNA, also designated SEQ ID:4439.

[58199] Another function of VGAM1728 is therefore inhibition of LOC92935 (Accession XM\_048197). Accordingly, utilities

of VGAM1728 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92935. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1729 (VGAM1729) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58200] VGAM1729 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1729 was detected is described hereinabove with reference to Figs. 1-8.

[58201] VGAM1729 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabies Virus. VGAM1729 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58202] VGAM1729 gene encodes a VGAM1729 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1729 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1729 precursor RNA is desig-

nated SEQ ID:1715, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1715 is located at position 8293 relative to the genome of Rabies Virus.

- [58203] VGAM1729 precursor RNA folds onto itself, forming VGAM1729 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [58204] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1729 folded precursor RNA into VGAM1729 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 60%) nucleotide sequence of VGAM1729 RNA is designated SEQ ID:4440, and is provided hereinbelow with reference to the sequence

listing part.

[58205] VGAM1729 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1729 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1729 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58206] VGAM1729 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1729 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1729 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1729 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1729 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58207] The complementary binding of VGAM1729 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1729 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1729 host target RNA into VGAM1729 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58208] It is appreciated that VGAM1729 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1729 host target genes. The mRNA of each one of this plurality of VGAM1729 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1729 RNA, herein designated VGAM

RNA, and which when bound by VGAM1729 RNA causes inhibition of translation of respective one or more VGAM1729 host target proteins.

[58209] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1729 gene, herein designated VGAM GENE, on one or more VGAM1729 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58210] It is yet further appreciated that a function of VGAM1729 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1729 include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGAM1729 correlate with, and may be deduced from, the identity of the host target genes which VGAM1729 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58211] Nucleotide sequences of the VGAM1729 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1729 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1729 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1729 are further described hereinbelow with reference to Table 1.

[58212] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1729 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1729 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58213] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1729 gene, herein designated VGAM is



inhibition of expression of VGAM1729 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1729 correlate with, and may be deduced from, the identity of the target genes which VGAM1729 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58214] Melanoma Antigen, Family C, 1 (MAGEC1, Accession NM\_005462) is a VGAM1729 host target gene. MAGEC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAGEC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAGEC1 BINDING SITE, designated SEQ ID:11945, to the nucleotide sequence of VGAM1729 RNA, herein designated VGAM RNA, also designated SEQ ID:4440.

[58215] A function of VGAM1729 is therefore inhibition of Melanoma Antigen, Family C, 1 (MAGEC1, Accession NM\_005462), a gene which is a member of the MAGE family C. Accordingly, utilities of VGAM1729 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAGEC1. The function of

MAGEC1 has been established by previous studies. Members of the MAGE (see OMIM Ref. No. MAGEA1, 300016), BAGE (OMIM Ref. No. 605167), and GAGE (see OMIM Ref. No. 604244) gene families are expressed in tumor cells and male germline cells and encode antigens recognized by cytotoxic T lymphocytes. These antigens are also known as CT antigens (see OMIM Ref. No. 300156) for their expression in cancer cells and testis. Lucas et al. (1998) used representational difference analysis to identify new CT antigen genes. They isolated a cDNA fragment showing homology to MAGE family genes. The fragment was used to isolate a full-length cDNA clone from an melanoma cell cDNA library. The MAGEC1 cDNA predicts a protein of 1,142 amino acids. MAGEC1 is 800 amino acids longer than other MAGE proteins due to the insertion of a large number of short repetitive sequences. RT-PCR analysis showed expression of MAGEC1 in tumors of a wide variety of histologic types, but expression was not seen in normal tissues, with the exception of testis. Lucas et al. (1998) determined that the MAGEC1 gene contains 4 exons and spans over 6 kb. Chen et al. (1998) screened an expression cDNA library constructed from a melanoma cell line with an allogeneic melanoma patient serum

known to contain antibodies against CT antigens. They isolated a cDNA encoding a new CT antigen, CT7, the sequence of which was more than 99% identical to that of MAGEC1 in the coding region.

[58216] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58217] Chen, Y.-T.; Gure, A. O.; Tsang, S.; Stockert, E.; Jager, E.; Knuth, A.; Old, L. J. : Identification of multiple cancer/testis antigens by allogeneic antibody screening of a melanoma cell line library. Proc. Nat. Acad. Sci. 95: 6919-6923, 1998. ; and

[58218] Lucas, S.; De Smet, C.; Arden, K. C.; Viars, C. S.; Lethe, B.; Lurquin, C.; Boon, T. : Identification of a new MAGE gene with tumor-specific expression by representational difference ana.

[58219] Further studies establishing the function and utilities of MAGEC1 are found in John Hopkins OMIM database record ID 300223, and in cited publications numbered 8802-8803 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Vinculin (VCL, Accession NM\_003373) is another VGAM1729 host target gene. VCL BINDING SITE1 and VCL BINDING SITE2

are HOST TARGET binding sites found in untranslated regions of mRNA encoded by VCL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VCL BINDING SITE1 and VCL BINDING SITE2, designated SEQ ID:9405 and SEQ ID:15194 respectively, to the nucleotide sequence of VGAM1729 RNA, herein designated VGAM RNA, also designated SEQ ID:4440.

[58220] Another function of VGAM1729 is therefore inhibition of Vinculin (VCL, Accession NM\_003373). Accordingly, utilities of VGAM1729 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VCL. KIAA1161 (Accession XM\_088501) is another VGAM1729 host target gene. KIAA1161 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1161 BINDING SITE, designated SEQ ID:39756, to the nucleotide sequence of VGAM1729 RNA, herein designated VGAM RNA, also designated SEQ ID:4440.

[58221] Another function of VGAM1729 is therefore inhibition of KIAA1161 (Accession XM\_088501). Accordingly, utilities of VGAM1729 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1161. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1730 (VGAM1730) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58222] VGAM1730 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1730 was detected is described hereinabove with reference to Figs. 1–8.

[58223] VGAM1730 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabies Virus. VGAM1730 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58224] VGAM1730 gene encodes a VGAM1730 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1730 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1730 precursor RNA is designated SEQ ID:1716, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1716 is located at position 6659 relative to the genome of Rabies Virus.

- [58225] VGAM1730 precursor RNA folds onto itself, forming VGAM1730 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [58226] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1730 folded precursor RNA into VGAM1730 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide se-

quence of VGAM1730 RNA is designated SEQ ID:4441, and is provided hereinbelow with reference to the sequence listing part.

[58227] VGAM1730 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1730 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1730 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58228] VGAM1730 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1730 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1730 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1730 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1730 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58229] The complementary binding of VGAM1730 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1730 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1730 host target RNA into VGAM1730 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58230] It is appreciated that VGAM1730 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1730 host target genes. The mRNA of each one of this plurality of VGAM1730 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1730 RNA, herein designated VGAM RNA, and which when bound by VGAM1730 RNA causes inhibition of translation of respective one or more VGAM1730 host target proteins.

[58231] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1730 gene, herein designated VGAM GENE, on one or more VGAM1730 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58232] It is yet further appreciated that a function of VGAM1730

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGAM1730 correlate with, and may be deduced from, the identity of the host target genes which VGAM1730 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58233] Nucleotide sequences of the VGAM1730 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1730 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1730 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1730 are further described hereinbelow with reference to Table 1.

[58234] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1730 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1730 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58235] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1730 gene, herein designated VGAM is inhibition of expression of VGAM1730 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1730 correlate with, and may be deduced from, the identity of the target genes which VGAM1730 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58236] Cadherin 18, Type 2 (CDH18, Accession NM\_004934) is a VGAM1730 host target gene. CDH18 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDH18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH18 BINDING SITE, designated SEQ ID:11380, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58237] A function of VGAM1730 is therefore inhibition of Cadherin 18, Type 2 (CDH18, Accession NM\_004934), a gene which mediates neural cell-cell interactions and may play an important role in neural development. Accordingly, utilities of VGAM1730 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with CDH18. The function of CDH18 has been established by previous studies. To isolate cDNAs encoding proteins that interact with beta-catenin, Shibata et al. (1997) screened a human adult brain cDNA expression library with recombinant beta-catenin protein. They identified a cDNA with high sequence homology to cadherin molecules and designated it cadherin-14 (CDH14), which has been renamed cadherin-18 (CDH18). Comparison of the deduced 790-amino acid CDH18 sequence with the sequences of other cadherins revealed that CDH18 is more closely related to type 2 cadherins than to type 1 cadherins, with the N-terminal regions of CDH18 and CDH12 (OMIM Ref. No. 600562) showing particularly high amino acid similarity. Northern blot analysis of human tissues detected 9.7-, 5.5-, and 3.9-kb CDH18 transcripts specifically in the central nervous system; CDH18 expression was also found in small-cell lung carcinoma cell lines, which have neuroectodermal cell phenotypes

[58238] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58239] Chalmers, I. J.; Hofler, H.; Atkinson, M. J. : Mapping of a

cadherin gene cluster to a region of chromosome 5 subject to frequent allelic loss in carcinoma. Genomics 57: 160–163, 1999. ; and

[58240] Shibata, T.; Shimoyama, Y.; Gotoh, M.; Hirohashi, S. : Identification of human cadherin–14, a novel neurally specific type II cadherin, by protein interaction cloning. J. Biol. Chem. 2.

[58241] Further studies establishing the function and utilities of CDH18 are found in John Hopkins OMIM database record ID 603019, and in cited publications numbered 587 and 8014 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM\_078470) is another VGAM1730 host target gene. COX15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX15 BINDING SITE, designated SEQ ID:27794, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58242] Another function of VGAM1730 is therefore inhibition of COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM\_078470). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX15. Dihydropyrimidinase-like 3 (DPYSL3, Accession NM\_001387) is another VGAM1730 host target gene. DPYSL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DPYSL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPYSL3 BINDING SITE, designated SEQ ID:7074, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58243] Another function of VGAM1730 is therefore inhibition of Dihydropyrimidinase-like 3 (DPYSL3, Accession NM\_001387), a gene which is a member of the dihydropyrimidinase family. Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYSL3. The function of DPYSL3 and its association with various diseases and

clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM24. Estrogen Receptor 1 (ESR1, Accession NM\_000125) is another VGAM1730 host target gene. ESR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESR1 BINDING SITE, designated SEQ ID:5601, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58244] Another function of VGAM1730 is therefore inhibition of Estrogen Receptor 1 (ESR1, Accession NM\_000125), a gene which involved in hormone-mediated inhibition of gene expression. Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESR1. The function of ESR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM695. Klotho (KL, Accession NM\_004795) is another VGAM1730 host target gene. KL BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by KL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KL BINDING SITE, designated SEQ ID:11204, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58245] Another function of VGAM1730 is therefore inhibition of Klotho (KL, Accession NM\_004795), a gene which has similarity to beta-glucosidases. Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KL. The function of KL has been established by previous studies. In a population-based association study, Arking et al. (2002) determined that allele 17 of microsatellite marker 1, which is 11 kb 3-prime of the last exon of the KL gene, is significantly more prevalent in Bohemian Czech newborns than in individuals more than 75 years old, independent of sex and health status. SSCP analysis identified another KL allele, which the authors termed KL-VS, defined by the presence of 6 single-nucleotide polymorphisms (SNPs) in an 800-bp region spanning exon 2 and flanking sequence. Allele-specific oligonucleotide hy-



bridization analysis showed complete linkage disequilibrium for the coding region mutations. Of the 3 mutations in exon 2, 1 is silent and 2 encode amino acid changes, phe352 to val (F352V) and cys370 to ser (C370S). The F352V mutation occurs at a completely conserved amino acid. Genotype analysis indicated that heterozygosity for F352V is significantly more prevalent in elderly Bohemians than in newborns, while homozygosity for V352, which is rare, is more prevalent in newborns. Kaplan–Meier survival analysis revealed that the heterozygote advantage promotes not only survival but also longevity (OMIM Ref. No. 152430) in elderly individuals more than 80 years old. Analysis of Caucasians and African Americans in Baltimore did not detect a heterozygote advantage for F352V, but did find decreased V352 homozygosity in the elderly. Western blot analysis of expression of the V352, S370, V352/S370, and wildtype alleles in HeLa cells or fibroblasts showed enhanced secretion of S370 mutant and decreased secretion of V352 variant compared with the 65–kD wildtype protein. The double mutant was secreted at intermediate levels, and the V352 mutant was most abundant intracellularly, suggesting a KL secretion defect. Functional analysis of a KL paralog, cytosolic beta–

glucosidase (CBGL1; 606619), which has a known substrate, p-nitrophenyl-beta-D-glucoside, established that a mutation (F289V) at the position in CBGL1 corresponding to KL F352V results in a complete loss of ability to cleave the substrate. Arking et al. (2002) concluded that the KL-VS mutation impairs the trafficking and catalytic activity of KL, which may in turn contribute to differences in the onset and severity of age-related phenotypes. They also suggested that additional deleterious mutations remained to be identified, since KL-VS is found on multiple marker allele haplotypes and is negatively associated with marker 1 allele 17. Animal model experiments lend further support to the function of KL. Mori et al. (2000) showed that klotho mice had a barely detectable amount of white adipose tissue, whereas brown adipose tissue (BAT) was comparably preserved. Although klotho mice consumed as much food as wildtype mice when normalized for body weight, they exhibited changes in parameters for energy homeostasis similar to those found under food-restricted conditions. The klotho mice had increased glucose tolerance and insulin sensitivity, as well as increased hepatic Pepck (OMIM Ref. No. 261680) expression. Levels of uncoupling protein-1 (UCP1; 113730) and body temperature

were significantly lower in klotho mice. Histologic analysis demonstrated lower glycogen, insulin, and lipid in the liver, pancreas, and BAT, respectively

[58246] It is appreciated that the abovementioned animal model for KL is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[58247] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58248] Mori, K.; Yahata, K.; Mukoyama, M.; Suganami, T.; Makino, H.; Nagae, T.; Masuzaki, H.; Ogawa, Y.; Sugawara, A.; Nabeshima, Y.; Nakao, K. : Disruption of klotho gene causes an abnormal energy homeostasis in mice. Biochem. Biophys. Res. Commun. 278: 665–670, 2000. ; and

[58249] Arking, D. E.; Krebsova, A.; Macek, M., Sr.; Macek, M., Jr.; Arking, A.; Mian, I. S.; Fried, L.; Hamosh, A.; Dey, S.; McIntosh, I.; Dietz, H. C. : Association of human aging with a func.

[58250] Further studies establishing the function and utilities of KL are found in John Hopkins OMIM database record ID 604824, and in cited publications numbered 5019–5024

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myeloid Cell Leukemia Sequence 1 (BCL2-related) (MCL1, Accession NM\_021960) is another VGAM1730 host target gene. MCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCL1 BINDING SITE, designated SEQ ID:22490, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58251] Another function of VGAM1730 is therefore inhibition of Myeloid Cell Leukemia Sequence 1 (BCL2-related) (MCL1, Accession NM\_021960), a gene which involved in programming of differentiation and concomitant maintenance of viability. Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCL1. The function of MCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1083. Mannosyl (alpha-1,3-)-glycoprotein Beta-

1,2-N-acetylglucosaminyltransferase (MGAT1, Accession NM\_002406) is another VGAM1730 host target gene. MGAT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGAT1 BINDING SITE, designated SEQ ID:8229, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58252] Another function of VGAM1730 is therefore inhibition of Mannosyl (alpha-1,3-)-glycoprotein Beta-1,2-N-acetylglucosaminyltransferase (MGAT1, Accession NM\_002406), a gene which exists as a single protein-encoding exon. Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT1. The function of MGAT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM165. Mannosyl (alpha-1,6-)-glycoprotein Beta-1,2-N-acetylglucosaminyltransferase (MGAT2, Accession

NM\_002408) is another VGAM1730 host target gene.

MGAT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGAT2 BINDING SITE, designated SEQ ID:8235, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58253] Another function of VGAM1730 is therefore inhibition of Mannosyl (alpha-1,6-)-glycoprotein Beta-1,2-N-acetylglucosaminyltransferase (MGAT2, Accession NM\_002408). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT2. SET Translocation (myeloid leukemia-associated) (SET, Accession NM\_003011) is another VGAM1730 host target gene. SET BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SET, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

SET BINDING SITE, designated SEQ ID:8923, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58254] Another function of VGAM1730 is therefore inhibition of SET Translocation (myeloid leukemia-associated) (SET, Accession NM\_003011). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SET. Angiomotin Like 1 (AMOTL1, Accession XM\_057045) is another VGAM1730 host target gene. AMOTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMOTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOTL1 BINDING SITE, designated SEQ ID:36470, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58255] Another function of VGAM1730 is therefore inhibition of Angiomotin Like 1 (AMOTL1, Accession XM\_057045). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOTL1. FLJ10901 (Accession

NM\_018265) is another VGAM1730 host target gene. FLJ10901 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10901, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10901 BINDING SITE, designated SEQ ID:20233, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58256] Another function of VGAM1730 is therefore inhibition of FLJ10901 (Accession NM\_018265). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10901. Nuclear Transcription Factor, X-box Binding 1 (NFX1, Accession NM\_002504) is another VGAM1730 host target gene. NFX1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NFX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFX1 BINDING SITE, designated SEQ ID:8328, to the nucleotide sequence of VGAM1730 RNA,



herein designated VGAM RNA, also designated SEQ ID:4441.

[58257] Another function of VGAM1730 is therefore inhibition of Nuclear Transcription Factor, X-box Binding 1 (NFX1, Accession NM\_002504). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFX1. PRO1914 (Accession NM\_014106) is another VGAM1730 host target gene. PRO1914 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1914, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1914 BINDING SITE, designated SEQ ID:15330, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58258] Another function of VGAM1730 is therefore inhibition of PRO1914 (Accession NM\_014106). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1914. PRO2000 (Accession NM\_014109) is another VGAM1730 host target gene. PRO2000 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO2000, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2000 BINDING SITE, designated SEQ ID:15338, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58259] Another function of VGAM1730 is therefore inhibition of PRO2000 (Accession NM\_014109). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2000. LOC149722 (Accession XM\_097709) is another VGAM1730 host target gene. LOC149722 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149722, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149722 BINDING SITE, designated SEQ ID:41046, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58260] Another function of VGAM1730 is therefore inhibition of

LOC149722 (Accession XM\_097709). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149722. LOC152992 (Accession XM\_087575) is another VGAM1730 host target gene. LOC152992 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152992 BINDING SITE, designated SEQ ID:39349, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58261] Another function of VGAM1730 is therefore inhibition of LOC152992 (Accession XM\_087575). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152992. LOC157663 (Accession XM\_088354) is another VGAM1730 host target gene. LOC157663 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC157663 BINDING SITE, designated SEQ ID:39640, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58262] Another function of VGAM1730 is therefore inhibition of LOC157663 (Accession XM\_088354). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157663. LOC245771 (Accession XM\_167366) is another VGAM1730 host target gene. LOC245771 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC245771, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245771 BINDING SITE, designated SEQ ID:44638, to the nucleotide sequence of VGAM1730 RNA, herein designated VGAM RNA, also designated SEQ ID:4441.

[58263] Another function of VGAM1730 is therefore inhibition of LOC245771 (Accession XM\_167366). Accordingly, utilities of VGAM1730 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245771. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1731 (VGAM1731) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58264] VGAM1731 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1731 was detected is described hereinabove with reference to Figs. 1–8.

[58265] VGAM1731 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabies Virus. VGAM1731 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58266] VGAM1731 gene encodes a VGAM1731 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1731 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1731 precursor RNA is designated SEQ ID:1717, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1717 is located at position 3422 relative to the

genome of Rabies Virus.

[58267] VGAM1731 precursor RNA folds onto itself, forming VGAM1731 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58268] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1731 folded precursor RNA into VGAM1731 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1731 RNA is designated SEQ ID:4442, and is provided hereinbelow with reference to the sequence listing part.

[58269] VGAM1731 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1731 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1731 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[58270] VGAM1731 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1731 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1731 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1731 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1731 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58271] The complementary binding of VGAM1731 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1731 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1731 host target RNA into VGAM1731 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58272] It is appreciated that VGAM1731 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1731 host target genes. The mRNA of each one of this plurality of VGAM1731 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1731 RNA, herein designated VGAM RNA, and which when bound by VGAM1731 RNA causes inhibition of translation of respective one or more VGAM1731 host target proteins.



[58273] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1731 gene, herein designated VGAM GENE, on one or more VGAM1731 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58274] It is yet further appreciated that a function of VGAM1731 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGAM1731 correlate

with, and may be deduced from, the identity of the host target genes which VGAM1731 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58275] Nucleotide sequences of the VGAM1731 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1731 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1731 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1731 are further described hereinbelow with reference to Table 1.

[58276] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1731 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1731 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58277] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1731 gene, herein designated VGAM is inhibition of expression of VGAM1731 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1731 correlate with, and may be deduced

from, the identity of the target genes which VGAM1731 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58278] Coagulation Factor VII (serum prothrombin conversion accelerator) (F7, Accession NM\_000131) is a VGAM1731 host target gene. F7 BINDING SITE1 and F7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by F7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F7 BINDING SITE1 and F7 BINDING SITE2, designated SEQ ID:5604 and SEQ ID:21233 respectively, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58279] A function of VGAM1731 is therefore inhibition of Coagulation Factor VII (serum prothrombin conversion accelerator) (F7, Accession NM\_000131). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F7. Thiamin Pyrophosphokinase 1 (TPK1, Accession NM\_022445) is another VGAM1731 host target gene. TPK1 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by TPK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPK1 BINDING SITE, designated SEQ ID:22780, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58280] Another function of VGAM1731 is therefore inhibition of Thiamin Pyrophosphokinase 1 (TPK1, Accession NM\_022445), a gene which catalyzes the conversion of thiamine, a form of vitamin B1, to thiamine pyrophosphate . Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPK1. The function of TPK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM475.DKFZP564M082 (Accession NM\_014042) is another VGAM1731 host target gene. DKFZP564M082 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP564M082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of DKFZP564M082 BINDING SITE, designated SEQ ID:15271, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58281] Another function of VGAM1731 is therefore inhibition of DKFZP564M082 (Accession NM\_014042). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564M082. FLJ13265 (Accession NM\_024877) is another VGAM1731 host target gene. FLJ13265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13265 BINDING SITE, designated SEQ ID:24312, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58282] Another function of VGAM1731 is therefore inhibition of FLJ13265 (Accession NM\_024877). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ13265. HSU79303 (Accession NM\_013301) is another VGAM1731 host target gene. HSU79303 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSU79303, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSU79303 BINDING SITE, designated SEQ ID:14962, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58283] Another function of VGAM1731 is therefore inhibition of HSU79303 (Accession NM\_013301). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSU79303. KIAA0472 (Accession XM\_050147) is another VGAM1731 host target gene. KIAA0472 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0472, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0472 BINDING SITE, designated SEQ ID:35574, to the nucleotide sequence of VGAM1731 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4442.

[58284] Another function of VGAM1731 is therefore inhibition of KIAA0472 (Accession XM\_050147). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0472. KIAA1237 (Accession XM\_087386) is another VGAM1731 host target gene. KIAA1237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1237 BINDING SITE, designated SEQ ID:39216, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58285] Another function of VGAM1731 is therefore inhibition of KIAA1237 (Accession XM\_087386). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1237. Paralemmin (PALM, Accession NM\_002579) is another VGAM1731 host target gene. PALM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PALM, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PALM BINDING SITE, designated SEQ ID:8439, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58286] Another function of VGAM1731 is therefore inhibition of Paralemmin (PALM, Accession NM\_002579). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PALM. LOC152445 (Accession XM\_098231) is another VGAM1731 host target gene. LOC152445 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152445 BINDING SITE, designated SEQ ID:41512, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58287] Another function of VGAM1731 is therefore inhibition of LOC152445 (Accession XM\_098231). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC152445. LOC157247 (Accession XM\_088275) is another VGAM1731 host target gene. LOC157247 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC157247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157247 BINDING SITE, designated SEQ ID:39578, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58288] Another function of VGAM1731 is therefore inhibition of LOC157247 (Accession XM\_088275). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157247. LOC219333 (Accession XM\_167944) is another VGAM1731 host target gene. LOC219333 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC219333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219333 BINDING SITE, designated SEQ ID:44934, to

the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58289] Another function of VGAM1731 is therefore inhibition of LOC219333 (Accession XM\_167944). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219333. LOC58489 (Accession XM\_051862) is another VGAM1731 host target gene. LOC58489 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC58489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58489 BINDING SITE, designated SEQ ID:35904, to the nucleotide sequence of VGAM1731 RNA, herein designated VGAM RNA, also designated SEQ ID:4442.

[58290] Another function of VGAM1731 is therefore inhibition of LOC58489 (Accession XM\_051862). Accordingly, utilities of VGAM1731 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58489. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1732 (VGAM1732) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58291] VGAM1732 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1732 was detected is described hereinabove with reference to Figs. 1–8.

[58292] VGAM1732 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabies Virus. VGAM1732 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58293] VGAM1732 gene encodes a VGAM1732 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1732 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1732 precursor RNA is designated SEQ ID:1718, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1718 is located at position 9788 relative to the genome of Rabies Virus.

[58294] VGAM1732 precursor RNA folds onto itself, forming

VGAM1732 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58295] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1732 folded precursor RNA into VGAM1732 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1732 RNA is designated SEQ ID:4443, and is provided hereinbelow with reference to the sequence listing part.

[58296] VGAM1732 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1732 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1732 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58297] VGAM1732 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1732 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1732 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1732 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1732 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58298] The complementary binding of VGAM1732 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1732 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1732 host target RNA into VGAM1732 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58299] It is appreciated that VGAM1732 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1732 host target genes. The mRNA of each one of this plurality of VGAM1732 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1732 RNA, herein designated VGAM RNA, and which when bound by VGAM1732 RNA causes inhibition of translation of respective one or more VGAM1732 host target proteins.

[58300] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1732 gene, herein designated VGAM GENE, on one or more VGAM1732 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58301] It is yet further appreciated that a function of VGAM1732 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGAM1732 correlate with, and may be deduced from, the identity of the host target genes which VGAM1732 binds and inhibits, and the

function of these host target genes, as elaborated herein–below.

[58302] Nucleotide sequences of the VGAM1732 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1732 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1732 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1732 are further described hereinbelow with reference to Table 1.

[58303] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM1732 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1732 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58304] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1732 gene, herein designated VGAM is inhibition of expression of VGAM1732 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1732 correlate with, and may be deduced from, the identity of the target genes which VGAM1732 binds and inhibits, and the function of these target genes,



as elaborated hereinbelow.

[58305] Paired Mesoderm Homeo Box 1 (PMX1, Accession NM\_006902) is a VGAM1732 host target gene. PMX1 BINDING SITE1 and PMX1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PMX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMX1 BINDING SITE1 and PMX1 BINDING SITE2, designated SEQ ID:13776 and SEQ ID:22911 respectively, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58306] A function of VGAM1732 is therefore inhibition of Paired Mesoderm Homeo Box 1 (PMX1, Accession NM\_006902), a gene which acts as a transcriptional regulator of muscle creatine kinase. Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMX1. The function of PMX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381.CDP-diacylglycerol--inositol

3-phosphatidyltransferase (phosphatidylinositol synthase) (CDIPT, Accession NM\_006319) is another VGAM1732 host target gene. CDIPT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDIPT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDIPT BINDING SITE, designated SEQ ID:13008, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58307] Another function of VGAM1732 is therefore inhibition of CDP-diacylglycerol--inositol 3-phosphatidyltransferase (phosphatidylinositol synthase) (CDIPT, Accession NM\_006319). Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDIPT. DJ328E19.C1.1 (Accession NM\_015383) is another VGAM1732 host target gene. DJ328E19.C1.1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ328E19.C1.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of DJ328E19.C1.1 BINDING SITE, designated SEQ ID:17682, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58308] Another function of VGAM1732 is therefore inhibition of DJ328E19.C1.1 (Accession NM\_015383). Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ328E19.C1.1. KIAA0408 (Accession NM\_014702) is another VGAM1732 host target gene. KIAA0408 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0408 BINDING SITE, designated SEQ ID:16229, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58309] Another function of VGAM1732 is therefore inhibition of KIAA0408 (Accession NM\_014702). Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0408. KIAA1005 (Accession XM\_051197) is another

VGAM1732 host target gene. KIAA1005 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1005, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1005 BINDING SITE, designated SEQ ID:35776, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58310] Another function of VGAM1732 is therefore inhibition of KIAA1005 (Accession XM\_051197). Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1005. KIAA1255 (Accession XM\_040626) is another VGAM1732 host target gene. KIAA1255 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1255, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1255 BINDING SITE, designated SEQ ID:33344, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58311] Another function of VGAM1732 is therefore inhibition of KIAA1255 (Accession XM\_040626). Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1255. NBR2 (Accession NM\_005821) is another VGAM1732 host target gene. NBR2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NBR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NBR2 BINDING SITE, designated SEQ ID:12423, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58312] Another function of VGAM1732 is therefore inhibition of NBR2 (Accession NM\_005821). Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBR2. RAB14, Member RAS Oncogene Family (RAB14, Accession NM\_016322) is another VGAM1732 host target gene. RAB14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB14, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB14 BINDING SITE, designated SEQ ID:18446, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58313] Another function of VGAM1732 is therefore inhibition of RAB14, Member RAS Oncogene Family (RAB14, Accession NM\_016322). Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB14. LOC137362 (Accession XM\_059905) is another VGAM1732 host target gene. LOC137362 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC137362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC137362 BINDING SITE, designated SEQ ID:37105, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58314] Another function of VGAM1732 is therefore inhibition of LOC137362 (Accession XM\_059905). Accordingly, utilities

of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC137362. LOC203025 (Accession XM\_114610) is another VGAM1732 host target gene. LOC203025 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203025 BINDING SITE, designated SEQ ID:43000, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58315] Another function of VGAM1732 is therefore inhibition of LOC203025 (Accession XM\_114610). Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203025. LOC90643 (Accession XM\_033145) is another VGAM1732 host target gene. LOC90643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC90643 BINDING SITE, designated SEQ ID:31850, to the nucleotide sequence of VGAM1732 RNA, herein designated VGAM RNA, also designated SEQ ID:4443.

[58316] Another function of VGAM1732 is therefore inhibition of LOC90643 (Accession XM\_033145). Accordingly, utilities of VGAM1732 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90643. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1733 (VGAM1733) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58317] VGAM1733 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1733 was detected is described hereinabove with reference to Figs. 1–8.

[58318] VGAM1733 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM1733 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.



[58319] VGAM1733 gene encodes a VGAM1733 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1733 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1733 precursor RNA is designated SEQ ID:1719, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1719 is located at position 40756 relative to the genome of Human Herpesvirus 3.

[58320] VGAM1733 precursor RNA folds onto itself, forming VGAM1733 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58321] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1733 folded precursor RNA into VGAM1733 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1733 RNA is designated SEQ ID:4444, and is provided hereinbelow with reference to the sequence listing part.

[58322] VGAM1733 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1733 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1733 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58323] VGAM1733 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1733 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1733 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1733 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1733 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58324] The complementary binding of VGAM1733 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1733 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1733 host target RNA into VGAM1733 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58325] It is appreciated that VGAM1733 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1733 host target genes. The mRNA of each one of this plurality of VGAM1733 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1733 RNA, herein designated VGAM RNA, and which when bound by VGAM1733 RNA causes inhibition of translation of respective one or more VGAM1733 host target proteins.

[58326] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1733 gene, herein designated VGAM GENE, on one or more VGAM1733 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58327] It is yet further appreciated that a function of VGAM1733 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1733 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1733 correlate with, and may be deduced from, the identity of the host target genes which VGAM1733 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58328] Nucleotide sequences of the VGAM1733 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1733 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1733 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1733 are further described hereinbelow with reference to Table 1.

[58329] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1733 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1733 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58330] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1733 gene, herein designated VGAM is inhibition of expression of VGAM1733 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1733 correlate with, and may be deduced from, the identity of the target genes which VGAM1733 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58331] Down-regulator of Transcription 1, TBP-binding (negative cofactor 2) (DR1, Accession XM\_002015) is a VGAM1733 host target gene. DR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DR1 BINDING SITE, designated SEQ ID:29857, to the nucleotide sequence of VGAM1733 RNA, herein designated VGAM RNA, also designated SEQ ID:4444.

[58332] A function of VGAM1733 is therefore inhibition of Down-regulator of Transcription 1, TBP-binding (negative cofactor 2) (DR1, Accession XM\_002015), a gene which influences functional repression of both activated and basal transcription of class ii genes. Accordingly, utilities of VGAM1733 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DR1. The function of DR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM711. Inositol Hexaphosphate Kinase 3 (IHPK3, Accession NM\_054111) is another VGAM1733 host target gene. IHPK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IHPK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IHPK3 BINDING SITE, designated SEQ ID:27656, to the nucleotide sequence of VGAM1733 RNA, herein designated VGAM RNA, also designated SEQ ID:4444.

[58333] Another function of VGAM1733 is therefore inhibition of Inositol Hexaphosphate Kinase 3 (IHPK3, Accession NM\_054111). Accordingly, utilities of VGAM1733 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with IHPK3. LOC123036 (Accession XM\_058676) is another VGAM1733 host target gene. LOC123036 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC123036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123036 BINDING SITE, designated SEQ ID:36716, to the nucleotide sequence of VGAM1733 RNA, herein designated VGAM RNA, also designated SEQ ID:4444.

[58334] Another function of VGAM1733 is therefore inhibition of LOC123036 (Accession XM\_058676). Accordingly, utilities of VGAM1733 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123036. LOC144962 (Accession XM\_084990) is another VGAM1733 host target gene. LOC144962 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences



of LOC144962 BINDING SITE, designated SEQ ID:37790, to the nucleotide sequence of VGAM1733 RNA, herein designated VGAM RNA, also designated SEQ ID:4444.

[58335] Another function of VGAM1733 is therefore inhibition of LOC144962 (Accession XM\_084990). Accordingly, utilities of VGAM1733 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144962. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1734 (VGAM1734) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58336] VGAM1734 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1734 was detected is described hereinabove with reference to Figs. 1–8.

[58337] VGAM1734 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM1734 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58338] VGAM1734 gene encodes a VGAM1734 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1734 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1734 precursor RNA is designated SEQ ID:1720, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1720 is located at position 35482 relative to the genome of Human Herpesvirus 3.

[58339] VGAM1734 precursor RNA folds onto itself, forming VGAM1734 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58340] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1734 folded precursor RNA into VGAM1734 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1734 RNA is designated SEQ ID:4445, and is provided hereinbelow with reference to the sequence listing part.

[58341] VGAM1734 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1734 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1734 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58342] VGAM1734 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1734 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1734 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1734 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1734 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58343] The complementary binding of VGAM1734 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1734 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1734 host target RNA into VGAM1734 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58344] It is appreciated that VGAM1734 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1734 host target genes. The mRNA of each one of this plurality of VGAM1734 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1734 RNA, herein designated VGAM RNA, and which when bound by VGAM1734 RNA causes inhibition of translation of respective one or more VGAM1734 host target proteins.

[58345] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1734 gene, herein designated VGAM GENE, on one or more VGAM1734 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[58346] It is yet further appreciated that a function of VGAM1734 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1734 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1734 correlate with, and may be deduced from, the identity of the host target genes which VGAM1734 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58347] Nucleotide sequences of the VGAM1734 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1734 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1734 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1734 are further described hereinbelow with reference to Table 1.

[58348] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1734 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1734 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58349] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1734 gene, herein designated VGAM is inhibition of expression of VGAM1734 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1734 correlate with, and may be deduced from, the identity of the target genes which VGAM1734 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58350] Acyl-Coenzyme A Dehydrogenase, Short/branched Chain (ACADSB, Accession NM\_001609) is a VGAM1734 host target gene. ACADSB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACADSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACADSB BINDING SITE, designated SEQ ID:7317, to the nucleotide sequence of VGAM1734 RNA, herein designated VGAM RNA, also designated SEQ ID:4445.

[58351] A function of VGAM1734 is therefore inhibition of Acyl-Coenzyme A Dehydrogenase, Short/branched Chain (ACADSB, Accession NM\_001609). Accordingly, utilities of VGAM1734 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACADSB. FLJ20331 (Accession NM\_017768) is another VGAM1734 host target gene. FLJ20331 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20331, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20331 BINDING SITE, designated SEQ ID:19385, to the nucleotide sequence of VGAM1734 RNA, herein designated VGAM RNA, also designated SEQ ID:4445.

[58352] Another function of VGAM1734 is therefore inhibition of FLJ20331 (Accession NM\_017768). Accordingly, utilities of VGAM1734 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20331. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1735 (VGAM1735) viral gene, which



modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58353] VGAM1735 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1735 was detected is described hereinabove with reference to Figs. 1–8.

[58354] VGAM1735 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM1735 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58355] VGAM1735 gene encodes a VGAM1735 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1735 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1735 precursor RNA is designated SEQ ID:1721, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1721 is located at position 33659 relative to the genome of Human Herpesvirus 3.

[58356] VGAM1735 precursor RNA folds onto itself, forming

VGAM1735 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58357] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1735 folded precursor RNA into VGAM1735 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1735 RNA is designated SEQ ID:4446, and is provided hereinbelow with reference to the sequence listing part.

[58358] VGAM1735 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1735 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1735 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58359] VGAM1735 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1735 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1735 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1735 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1735 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58360] The complementary binding of VGAM1735 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1735 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1735 host target RNA into VGAM1735 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58361] It is appreciated that VGAM1735 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1735 host target genes. The mRNA of each one of this plurality of VGAM1735 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1735 RNA, herein designated VGAM RNA, and which when bound by VGAM1735 RNA causes inhibition of translation of respective one or more VGAM1735 host target proteins.

[58362] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1735 gene, herein designated VGAM GENE, on one or more VGAM1735 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58363] It is yet further appreciated that a function of VGAM1735 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1735 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1735 correlate with, and may be deduced from, the identity of the host target genes which VGAM1735 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[58364] Nucleotide sequences of the VGAM1735 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1735 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1735 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1735 are further described hereinbelow with reference to Table 1.

[58365] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1735 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1735 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58366] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1735 gene, herein designated VGAM is inhibition of expression of VGAM1735 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1735 correlate with, and may be deduced from, the identity of the target genes which VGAM1735 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[58367] MSTP032 (Accession NM\_025226) is a VGAM1735 host target gene. MSTP032 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MSTP032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSTP032 BINDING SITE, designated SEQ ID:24904, to the nucleotide sequence of VGAM1735 RNA, herein designated VGAM RNA, also designated SEQ ID:4446.

[58368] A function of VGAM1735 is therefore inhibition of MSTP032 (Accession NM\_025226). Accordingly, utilities of VGAM1735 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSTP032. Serum/glucocorticoid Regulated Kinase-like (SGKL, Accession NM\_013257) is another VGAM1735 host target gene. SGKL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SGKL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SGKL BINDING SITE, designated SEQ

ID:14927, to the nucleotide sequence of VGAM1735 RNA, herein designated VGAM RNA, also designated SEQ ID:4446.

[58369] Another function of VGAM1735 is therefore inhibition of Serum/glucocorticoid Regulated Kinase-like (SGKL, Accession NM\_013257). Accordingly, utilities of VGAM1735 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SGKL. LOC149401 (Accession XM\_086511) is another VGAM1735 host target gene. LOC149401 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149401 BINDING SITE, designated SEQ ID:38736, to the nucleotide sequence of VGAM1735 RNA, herein designated VGAM RNA, also designated SEQ ID:4446.

[58370] Another function of VGAM1735 is therefore inhibition of LOC149401 (Accession XM\_086511). Accordingly, utilities of VGAM1735 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149401. Fig. 1 further provides a conceptual descrip-



tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1736 (VGAM1736) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58371] VGAM1736 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1736 was detected is described hereinabove with reference to Figs. 1–8.

[58372] VGAM1736 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM1736 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58373] VGAM1736 gene encodes a VGAM1736 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1736 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1736 precursor RNA is designated SEQ ID:1722, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1722 is located at position 39181 relative to the genome of Human Herpesvirus 3.

[58374] VGAM1736 precursor RNA folds onto itself, forming VGAM1736 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58375] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1736 folded precursor RNA into VGAM1736 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1736 RNA is designated SEQ ID:4447, and is provided hereinbelow with reference to the sequence listing part.

[58376] VGAM1736 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1736 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1736 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58377] VGAM1736 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1736 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1736 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1736 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1736 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[58378] The complementary binding of VGAM1736 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1736 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1736 host target RNA into VGAM1736 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58379] It is appreciated that VGAM1736 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1736 host target genes. The mRNA of each one of this plurality of VGAM1736 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1736 RNA, herein designated VGAM RNA, and which when bound by VGAM1736 RNA causes inhibition of translation of respective one or more

VGAM1736 host target proteins.

[58380] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1736 gene, herein designated VGAM GENE, on one or more VGAM1736 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58381] It is yet further appreciated that a function of VGAM1736 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1736 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Spe-

cific functions, and accordingly utilities, of VGAM1736 correlate with, and may be deduced from, the identity of the host target genes which VGAM1736 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58382] Nucleotide sequences of the VGAM1736 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1736 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1736 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1736 are further described hereinbelow with reference to Table 1.

[58383] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1736 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1736 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58384] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1736 gene, herein designated VGAM is inhibition of expression of VGAM1736 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1736 correlate with, and may be deduced from, the identity of the target genes which VGAM1736 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58385] F-box and Leucine-rich Repeat Protein 3A (FBXL3A, Accession NM\_012158) is a VGAM1736 host target gene. FBXL3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXL3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXL3A BINDING SITE, designated SEQ ID:14455, to the nucleotide sequence of VGAM1736 RNA, herein designated VGAM RNA, also designated SEQ ID:4447.

[58386] A function of VGAM1736 is therefore inhibition of F-box and Leucine-rich Repeat Protein 3A (FBXL3A, Accession NM\_012158), a gene which is a putative SCF ubiquitin ligase subunit involved in protein degradation. Accordingly, utilities of VGAM1736 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXL3A. The function of FBXL3A and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM1172. Glucagon-like Peptide 1 Receptor (GLP1R, Accession NM\_002062) is another VGAM1736 host target gene. GLP1R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLP1R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLP1R BINDING SITE, designated SEQ ID:7829, to the nucleotide sequence of VGAM1736 RNA, herein designated VGAM RNA, also designated SEQ ID:4447.

[58387] Another function of VGAM1736 is therefore inhibition of Glucagon-like Peptide 1 Receptor (GLP1R, Accession NM\_002062), a gene which is mediated by g proteins which activate adenylyl cyclase. Accordingly, utilities of VGAM1736 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLP1R. The function of GLP1R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1652. Transcription Factor 8 (represses interleukin 2 expression) (TCF8, Accession NM\_030751) is an-



other VGAM1736 host target gene. TCF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF8 BINDING SITE, designated SEQ ID:25039, to the nucleotide sequence of VGAM1736 RNA, herein designated VGAM RNA, also designated SEQ ID:4447.

[58388] Another function of VGAM1736 is therefore inhibition of Transcription Factor 8 (represses interleukin 2 expression) (TCF8, Accession NM\_030751), a gene which may be responsible for transcriptional repression of the il-2 gene and regulates the promoter activity of the atp1a1 gene . Accordingly, utilities of VGAM1736 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF8. The function of TCF8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM166. G-rich RNA Sequence Binding Factor 1 (GRSF1, Accession NM\_002092) is another VGAM1736 host target gene. GRSF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by GRSF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRSF1 BINDING SITE, designated SEQ ID:7881, to the nucleotide sequence of VGAM1736 RNA, herein designated VGAM RNA, also designated SEQ ID:4447.

[58389] Another function of VGAM1736 is therefore inhibition of G-rich RNA Sequence Binding Factor 1 (GRSF1, Accession NM\_002092). Accordingly, utilities of VGAM1736 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRSF1. KIAA0416 (Accession NM\_015564) is another VGAM1736 host target gene. KIAA0416 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0416 BINDING SITE, designated SEQ ID:17840, to the nucleotide sequence of VGAM1736 RNA, herein designated VGAM RNA, also designated SEQ ID:4447.

[58390] Another function of VGAM1736 is therefore inhibition of

KIAA0416 (Accession NM\_015564). Accordingly, utilities of VGAM1736 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0416. SCDGF-B (Accession NM\_025208) is another VGAM1736 host target gene. SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SCDGF-B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2, designated SEQ ID:24878 and SEQ ID:26980 respectively, to the nucleotide sequence of VGAM1736 RNA, herein designated VGAM RNA, also designated SEQ ID:4447.

[58391] Another function of VGAM1736 is therefore inhibition of SCDGF-B (Accession NM\_025208). Accordingly, utilities of VGAM1736 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCDGF-B. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1737 (VGAM1737) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58392] VGAM1737 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1737 was detected is described hereinabove with reference to Figs. 1–8.

[58393] VGAM1737 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM1737 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58394] VGAM1737 gene encodes a VGAM1737 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1737 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1737 precursor RNA is designated SEQ ID:1723, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1723 is located at position 32691 relative to the genome of Human Herpesvirus 3.

[58395] VGAM1737 precursor RNA folds onto itself, forming

VGAM1737 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58396] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1737 folded precursor RNA into VGAM1737 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1737 RNA is designated SEQ ID:4448, and is provided hereinbelow with reference to the sequence listing part.

[58397] VGAM1737 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1737 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1737 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58398] VGAM1737 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1737 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1737 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1737 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1737 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58399] The complementary binding of VGAM1737 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1737 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1737 host target RNA into VGAM1737 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58400] It is appreciated that VGAM1737 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1737 host target genes. The mRNA of each one of this plurality of VGAM1737 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1737 RNA, herein designated VGAM RNA, and which when bound by VGAM1737 RNA causes inhibition of translation of respective one or more VGAM1737 host target proteins.

[58401] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1737 gene, herein designated VGAM GENE, on one or more VGAM1737 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58402] It is yet further appreciated that a function of VGAM1737 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1737 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1737 correlate with, and may be deduced from, the identity of the host target genes which VGAM1737 binds and in-



hibits, and the function of these host target genes, as elaborated hereinbelow.

[58403] Nucleotide sequences of the VGAM1737 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1737 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1737 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1737 are further described hereinbelow with reference to Table 1.

[58404] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1737 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1737 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58405] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1737 gene, herein designated VGAM is inhibition of expression of VGAM1737 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1737 correlate with, and may be deduced from, the identity of the target genes which VGAM1737 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[58406] Contactin Associated Protein-like 2 (CNTNAP2, Accession NM\_014141) is a VGAM1737 host target gene. CNTNAP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNTNAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNTNAP2 BINDING SITE, designated SEQ ID:15417, to the nucleotide sequence of VGAM1737 RNA, herein designated VGAM RNA, also designated SEQ ID:4448.

[58407] A function of VGAM1737 is therefore inhibition of Contactin Associated Protein-like 2 (CNTNAP2, Accession NM\_014141). Accordingly, utilities of VGAM1737 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNTNAP2. F-box and Leucine-rich Repeat Protein 11 (FBXL11, Accession NM\_012308) is another VGAM1737 host target gene. FBXL11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FBXL11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of FBXL11 BINDING SITE, designated SEQ ID:14678, to the nucleotide sequence of VGAM1737 RNA, herein designated VGAM RNA, also designated SEQ ID:4448.

[58408] Another function of VGAM1737 is therefore inhibition of F-box and Leucine-rich Repeat Protein 11 (FBXL11, Accession NM\_012308), a gene which are BTB/POZ domain-containing zinc finger proteins implicated in oncogenesis. Accordingly, utilities of VGAM1737 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXL11. The function of FBXL11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM404. Protein Kinase C and Casein Kinase Substrate In Neurons 1 (PACSIN1, Accession XM\_166424) is another VGAM1737 host target gene. PACSIN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACSIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACSIN1 BINDING SITE,

designated SEQ ID:44314, to the nucleotide sequence of VGAM1737 RNA, herein designated VGAM RNA, also designated SEQ ID:4448.

[58409] Another function of VGAM1737 is therefore inhibition of Protein Kinase C and Casein Kinase Substrate In Neurons 1 (PACSIN1, Accession XM\_166424). Accordingly, utilities of VGAM1737 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACSIN1. FLJ11850 (Accession NM\_022741) is another VGAM1737 host target gene. FLJ11850 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11850, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11850 BINDING SITE, designated SEQ ID:22947, to the nucleotide sequence of VGAM1737 RNA, herein designated VGAM RNA, also designated SEQ ID:4448.

[58410] Another function of VGAM1737 is therefore inhibition of FLJ11850 (Accession NM\_022741). Accordingly, utilities of VGAM1737 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11850. KIAA0255 (Accession NM\_014742) is another

VGAM1737 host target gene. KIAA0255 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0255, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0255 BINDING SITE, designated SEQ ID:16415, to the nucleotide sequence of VGAM1737 RNA, herein designated VGAM RNA, also designated SEQ ID:4448.

[58411] Another function of VGAM1737 is therefore inhibition of KIAA0255 (Accession NM\_014742). Accordingly, utilities of VGAM1737 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0255. RAN Binding Protein 6 (RANBP6, Accession XM\_029423) is another VGAM1737 host target gene. RANBP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RANBP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RANBP6 BINDING SITE, designated SEQ ID:30884, to the nucleotide sequence of VGAM1737 RNA, herein designated VGAM RNA, also designated SEQ

ID:4448.

[58412] Another function of VGAM1737 is therefore inhibition of RAN Binding Protein 6 (RANBP6, Accession XM\_029423). Accordingly, utilities of VGAM1737 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RANBP6. LOC157798 (Accession XM\_098827) is another VGAM1737 host target gene. LOC157798 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157798 BINDING SITE, designated SEQ ID:41847, to the nucleotide sequence of VGAM1737 RNA, herein designated VGAM RNA, also designated SEQ ID:4448.

[58413] Another function of VGAM1737 is therefore inhibition of LOC157798 (Accession XM\_098827). Accordingly, utilities of VGAM1737 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157798. LOC221715 (Accession XM\_168092) is another VGAM1737 host target gene. LOC221715 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC221715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221715 BINDING SITE, designated SEQ ID:45016, to the nucleotide sequence of VGAM1737 RNA, herein designated VGAM RNA, also designated SEQ ID:4448.

[58414] Another function of VGAM1737 is therefore inhibition of LOC221715 (Accession XM\_168092). Accordingly, utilities of VGAM1737 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221715. LOC254659 (Accession XM\_170822) is another VGAM1737 host target gene. LOC254659 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254659, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254659 BINDING SITE, designated SEQ ID:45600, to the nucleotide sequence of VGAM1737 RNA, herein designated VGAM RNA, also designated SEQ ID:4448.

[58415] Another function of VGAM1737 is therefore inhibition of LOC254659 (Accession XM\_170822). Accordingly, utilities

of VGAM1737 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254659. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1738 (VGAM1738) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58416] VGAM1738 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1738 was detected is described hereinabove with reference to Figs. 1-8.

[58417] VGAM1738 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM1738 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58418] VGAM1738 gene encodes a VGAM1738 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1738 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-



cleotide sequence of VGAM1738 precursor RNA is designated SEQ ID:1724, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1724 is located at position 41710 relative to the genome of Human Herpesvirus 3.

[58419] VGAM1738 precursor RNA folds onto itself, forming VGAM1738 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58420] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1738 folded precursor RNA into VGAM1738 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1738 RNA is designated SEQ ID:4449, and

is provided hereinbelow with reference to the sequence listing part.

[58421] VGAM1738 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1738 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1738 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[58422] VGAM1738 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1738 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1738 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1738 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1738 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58423] The complementary binding of VGAM1738 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1738 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1738 host target RNA into VGAM1738 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58424] It is appreciated that VGAM1738 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1738 host target genes. The mRNA of each one of this plurality of VGAM1738 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1738 RNA, herein designated VGAM RNA, and which when bound by VGAM1738 RNA causes inhibition of translation of respective one or more VGAM1738 host target proteins.

[58425] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1738 gene, herein designated VGAM GENE, on one or more VGAM1738 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58426] It is yet further appreciated that a function of VGAM1738 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1738 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1738 correlate with, and may be deduced from, the identity of the host target genes which VGAM1738 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58427] Nucleotide sequences of the VGAM1738 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1738 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1738 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1738 are further described hereinbelow with reference to Table 1.

[58428] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1738 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1738 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58429] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1738 gene, herein designated VGAM is inhibition of expression of VGAM1738 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1738 correlate with, and may be deduced from, the identity of the target genes which VGAM1738 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58430] Extracellular Matrix Protein 2, Female Organ and Adipocyte Specific (ECM2, Accession NM\_001393) is a VGAM1738 host target gene. ECM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ECM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ECM2 BINDING SITE, designated SEQ ID:7086, to the nucleotide sequence of VGAM1738 RNA, herein designated VGAM RNA, also designated SEQ ID:4449.

[58431] A function of VGAM1738 is therefore inhibition of Extracellular Matrix Protein 2, Female Organ and Adipocyte Specific (ECM2, Accession NM\_001393). Accordingly, utilities of VGAM1738 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with ECM2. Epsin 2 (EPN2, Accession NM\_014964) is another VGAM1738 host target gene. EPN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPN2 BINDING SITE, designated SEQ ID:17344, to the nucleotide sequence of VGAM1738 RNA, herein designated VGAM RNA, also designated SEQ ID:4449.

[58432] Another function of VGAM1738 is therefore inhibition of Epsin 2 (EPN2, Accession NM\_014964). Accordingly, utilities of VGAM1738 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPN2. RAB39, Member RAS Oncogene Family (RAB39, Accession XM\_084662) is another VGAM1738 host target gene. RAB39 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB39 BINDING SITE, designated SEQ ID:37643, to the nucleotide sequence of VGAM1738 RNA,

herein designated VGAM RNA, also designated SEQ ID:4449.

[58433] Another function of VGAM1738 is therefore inhibition of RAB39, Member RAS Oncogene Family (RAB39, Accession XM\_084662). Accordingly, utilities of VGAM1738 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB39. LOC151473 (Accession XM\_087215) is another VGAM1738 host target gene. LOC151473 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151473, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151473 BINDING SITE, designated SEQ ID:39118, to the nucleotide sequence of VGAM1738 RNA, herein designated VGAM RNA, also designated SEQ ID:4449.

[58434] Another function of VGAM1738 is therefore inhibition of LOC151473 (Accession XM\_087215). Accordingly, utilities of VGAM1738 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151473. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the



present invention, referred to here as Viral Genomic Address Messenger 1739 (VGAM1739) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58435] VGAM1739 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1739 was detected is described hereinabove with reference to Figs. 1–8.

[58436] VGAM1739 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM1739 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58437] VGAM1739 gene encodes a VGAM1739 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1739 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1739 precursor RNA is designated SEQ ID:1725, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1725 is located at position 38932 relative to the

genome of Human Herpesvirus 3.

[58438] VGAM1739 precursor RNA folds onto itself, forming VGAM1739 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58439] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1739 folded precursor RNA into VGAM1739 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 62%) nucleotide sequence of VGAM1739 RNA is designated SEQ ID:4450, and is provided hereinbelow with reference to the sequence listing part.

[58440] VGAM1739 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1739 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1739 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[58441] VGAM1739 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1739 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1739 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1739 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1739 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58442] The complementary binding of VGAM1739 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1739 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1739 host target RNA into VGAM1739 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58443] It is appreciated that VGAM1739 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1739 host target genes. The mRNA of each one of this plurality of VGAM1739 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1739 RNA, herein designated VGAM RNA, and which when bound by VGAM1739 RNA causes inhibition of translation of respective one or more VGAM1739 host target proteins.

[58444] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1739 gene, herein designated VGAM GENE, on one or more VGAM1739 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58445] It is yet further appreciated that a function of VGAM1739 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1739

correlate with, and may be deduced from, the identity of the host target genes which VGAM1739 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58446] Nucleotide sequences of the VGAM1739 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1739 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1739 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1739 are further described hereinbelow with reference to Table 1.

[58447] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1739 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1739 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58448] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1739 gene, herein designated VGAM is inhibition of expression of VGAM1739 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1739 correlate with, and may be deduced

from, the identity of the target genes which VGAM1739 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58449] ADP-ribosylation Factor 4-like (ARF4L, Accession XM\_045890) is a VGAM1739 host target gene. ARF4L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARF4L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARF4L BINDING SITE, designated SEQ ID:34603, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58450] A function of VGAM1739 is therefore inhibition of ADP-ribosylation Factor 4-like (ARF4L, Accession XM\_045890). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARF4L. Copine III (CPNE3, Accession NM\_003909) is another VGAM1739 host target gene. CPNE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPNE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of CPNE3 BINDING SITE, designated SEQ ID:9993, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58451] Another function of VGAM1739 is therefore inhibition of Copine III (CPNE3, Accession NM\_003909), a gene which may function in membrane trafficking. Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPNE3. The function of CPNE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. Filamin B, Beta (actin binding protein 278) (FLNB, Accession XM\_030806) is another VGAM1739 host target gene. FLNB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLNB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLNB BINDING SITE, designated SEQ ID:31143, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.



[58452] Another function of VGAM1739 is therefore inhibition of Filamin B, Beta (actin binding protein 278) (FLNB, Accession XM\_030806), a gene which Filamin B, beta; binds actin, interacts with cytoplasmic domain of Ibalpha. Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLNB. The function of FLNB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM416. SMURF1 (Accession XM\_166483) is another VGAM1739 host target gene. SMURF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMURF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMURF1 BINDING SITE, designated SEQ ID:44413, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58453] Another function of VGAM1739 is therefore inhibition of SMURF1 (Accession XM\_166483). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SMURF1. Forkhead Box J1 (FOXJ1, Accession NM\_001454) is another VGAM1739 host target gene. FOXJ1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FOXJ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXJ1 BINDING SITE, designated SEQ ID:7188, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58454] Another function of VGAM1739 is therefore inhibition of Forkhead Box J1 (FOXJ1, Accession NM\_001454). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXJ1. GRO3 (Accession XM\_031287) is another VGAM1739 host target gene. GRO3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRO3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRO3 BINDING SITE, designated SEQ ID:31334, to the nucleotide sequence of

VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58455] Another function of VGAM1739 is therefore inhibition of GRO3 (Accession XM\_031287). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRO3. Hippocalcin Like 4 (HPCAL4, Accession NM\_016257) is another VGAM1739 host target gene. HPCAL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPCAL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPCAL4 BINDING SITE, designated SEQ ID:18386, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58456] Another function of VGAM1739 is therefore inhibition of Hippocalcin Like 4 (HPCAL4, Accession NM\_016257). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPCAL4. Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM\_014424) is another VGAM1739 host target gene.

HSPB7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPB7 BINDING SITE, designated SEQ ID:15779, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58457] Another function of VGAM1739 is therefore inhibition of Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM\_014424). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPB7. HSPC144 (Accession NM\_014174) is another VGAM1739 host target gene. HSPC144 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPC144, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC144 BINDING SITE, designated SEQ ID:15462, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM

RNA, also designated SEQ ID:4450.

[58458] Another function of VGAM1739 is therefore inhibition of HSPC144 (Accession NM\_014174). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC144. KIAA0433 (Accession NM\_015216) is another VGAM1739 host target gene. KIAA0433 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0433, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0433 BINDING SITE, designated SEQ ID:17550, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58459] Another function of VGAM1739 is therefore inhibition of KIAA0433 (Accession NM\_015216). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0433. KIAA1084 (Accession NM\_014910) is another VGAM1739 host target gene. KIAA1084 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1084, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1084 BINDING SITE, designated SEQ ID:17137, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58460] Another function of VGAM1739 is therefore inhibition of KIAA1084 (Accession NM\_014910). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1084. LOC90750 (Accession XM\_033868) is another VGAM1739 host target gene. LOC90750 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90750 BINDING SITE, designated SEQ ID:31965, to the nucleotide sequence of VGAM1739 RNA, herein designated VGAM RNA, also designated SEQ ID:4450.

[58461] Another function of VGAM1739 is therefore inhibition of LOC90750 (Accession XM\_033868). Accordingly, utilities of VGAM1739 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC90750. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1740 (VGAM1740) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58462] VGAM1740 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1740 was detected is described hereinabove with reference to Figs. 1–8.

[58463] VGAM1740 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM1740 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58464] VGAM1740 gene encodes a VGAM1740 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1740 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1740 precursor RNA is desig-

nated SEQ ID:1726, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1726 is located at position 36839 relative to the genome of Human Herpesvirus 3.

- [58465] VGAM1740 precursor RNA folds onto itself, forming VGAM1740 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [58466] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1740 folded precursor RNA into VGAM1740 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1740 RNA is designated SEQ ID:4451, and is provided hereinbelow with reference to the sequence



listing part.

[58467] VGAM1740 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1740 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1740 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58468] VGAM1740 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1740 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1740 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1740 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1740 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58469] The complementary binding of VGAM1740 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1740 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1740 host target RNA into VGAM1740 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58470] It is appreciated that VGAM1740 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1740 host target genes. The mRNA of each one of this plurality of VGAM1740 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1740 RNA, herein designated VGAM

RNA, and which when bound by VGAM1740 RNA causes inhibition of translation of respective one or more VGAM1740 host target proteins.

[58471] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1740 gene, herein designated VGAM GENE, on one or more VGAM1740 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58472] It is yet further appreciated that a function of VGAM1740 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1740 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1740 correlate with, and may be deduced from, the identity of the host target genes which VGAM1740 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58473] Nucleotide sequences of the VGAM1740 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1740 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1740 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1740 are further described hereinbelow with reference to Table 1.

[58474] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1740 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1740 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58475] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1740 gene, herein designated VGAM is

inhibition of expression of VGAM1740 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1740 correlate with, and may be deduced from, the identity of the target genes which VGAM1740 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58476] Ceroid-lipofuscinosis, Neuronal 5 (CLN5, Accession NM\_006493) is a VGAM1740 host target gene. CLN5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN5 BINDING SITE, designated SEQ ID:13233, to the nucleotide sequence of VGAM1740 RNA, herein designated VGAM RNA, also designated SEQ ID:4451.

[58477] A function of VGAM1740 is therefore inhibition of Ceroid-lipofuscinosis, Neuronal 5 (CLN5, Accession NM\_006493). Accordingly, utilities of VGAM1740 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN5. COX11 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX11, Accession NM\_004375) is another VGAM1740 host target gene.

COX11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COX11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX11 BINDING SITE, designated SEQ ID:10597, to the nucleotide sequence of VGAM1740 RNA, herein designated VGAM RNA, also designated SEQ ID:4451.

[58478] Another function of VGAM1740 is therefore inhibition of COX11 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX11, Accession NM\_004375). Accordingly, utilities of VGAM1740 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX11. SON DNA Binding Protein (SON, Accession NM\_138926) is another VGAM1740 host target gene. SON BINDING SITE1 through SON BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SON, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SON BINDING SITE1 through SON BINDING SITE3, designated SEQ ID:29043,

SEQ ID:27747 and SEQ ID:29047 respectively, to the nucleotide sequence of VGAM1740 RNA, herein designated VGAM RNA, also designated SEQ ID:4451.

[58479] Another function of VGAM1740 is therefore inhibition of SON DNA Binding Protein (SON, Accession NM\_138926). Accordingly, utilities of VGAM1740 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SON. X-box Binding Protein 1 (XBP1, Accession NM\_005080) is another VGAM1740 host target gene. XBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XBP1 BINDING SITE, designated SEQ ID:11532, to the nucleotide sequence of VGAM1740 RNA, herein designated VGAM RNA, also designated SEQ ID:4451.

[58480] Another function of VGAM1740 is therefore inhibition of X-box Binding Protein 1 (XBP1, Accession NM\_005080), a gene which has a role in transcriptional regulation. Accordingly, utilities of VGAM1740 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XBP1. The function of XBP1 and its associ-

ation with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM746.DJ37E16.5 (Accession NM\_020315) is another VGAM1740 host target gene.

DJ37E16.5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ37E16.5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ37E16.5 BINDING SITE, designated SEQ ID:21574, to the nucleotide sequence of VGAM1740 RNA, herein designated VGAM RNA, also designated SEQ ID:4451.

[58481] Another function of VGAM1740 is therefore inhibition of DJ37E16.5 (Accession NM\_020315). Accordingly, utilities of VGAM1740 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ37E16.5. KIAA1456 (Accession XM\_040100) is another VGAM1740 host target gene. KIAA1456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the



complementarity of the nucleotide sequences of KIAA1456 BINDING SITE, designated SEQ ID:33266, to the nucleotide sequence of VGAM1740 RNA, herein designated VGAM RNA, also designated SEQ ID:4451.

[58482] Another function of VGAM1740 is therefore inhibition of KIAA1456 (Accession XM\_040100). Accordingly, utilities of VGAM1740 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1456. TUCAN (Accession NM\_014959) is another VGAM1740 host target gene. TUCAN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUCAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUCAN BINDING SITE, designated SEQ ID:17321, to the nucleotide sequence of VGAM1740 RNA, herein designated VGAM RNA, also designated SEQ ID:4451.

[58483] Another function of VGAM1740 is therefore inhibition of TUCAN (Accession NM\_014959). Accordingly, utilities of VGAM1740 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUCAN. LOC158310 (Accession XM\_098919) is another

VGAM1740 host target gene. LOC158310 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158310 BINDING SITE, designated SEQ ID:41950, to the nucleotide sequence of VGAM1740 RNA, herein designated VGAM RNA, also designated SEQ ID:4451.

[58484] Another function of VGAM1740 is therefore inhibition of LOC158310 (Accession XM\_098919). Accordingly, utilities of VGAM1740 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158310. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1741 (VGAM1741) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58485] VGAM1741 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1741 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[58486] VGAM1741 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1741 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58487] VGAM1741 gene encodes a VGAM1741 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1741 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1741 precursor RNA is designated SEQ ID:1727, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1727 is located at position 36070 relative to the genome of Cercopithecine Herpesvirus 7.

[58488] VGAM1741 precursor RNA folds onto itself, forming VGAM1741 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58489] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1741 folded precursor RNA into VGAM1741 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1741 RNA is designated SEQ ID:4452, and is provided hereinbelow with reference to the sequence listing part.

[58490] VGAM1741 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1741 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1741 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58491] VGAM1741 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1741 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1741 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1741 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1741 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58492] The complementary binding of VGAM1741 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1741 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1741 host target RNA into VGAM1741 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58493] It is appreciated that VGAM1741 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1741 host target genes. The mRNA of each one of this plurality of VGAM1741 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1741 RNA, herein designated VGAM RNA, and which when bound by VGAM1741 RNA causes inhibition of translation of respective one or more VGAM1741 host target proteins.

[58494] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1741 gene, herein designated VGAM GENE, on one or more VGAM1741 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58495] It is yet further appreciated that a function of VGAM1741 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1741 correlate with, and may be deduced from, the identity of the host target genes which VGAM1741 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58496] Nucleotide sequences of the VGAM1741 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1741 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1741 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1741 are further described hereinbelow with reference to Table 1.

[58497] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1741 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1741 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58498] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1741 gene, herein designated VGAM is inhibition of expression of VGAM1741 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1741 correlate with, and may be deduced from, the identity of the target genes which VGAM1741 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58499] 1-acylglycerol-3-phosphate O-acyltransferase 2 (lysophosphatidic acid acyltransferase, beta) (AGPAT2, Accession XM\_038030) is a VGAM1741 host target gene. AGPAT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AG-



PAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGPAT2 BINDING SITE, designated SEQ ID:32744, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58500] A function of VGAM1741 is therefore inhibition of 1-acylglycerol-3-phosphate O-acyltransferase 2 (lysophosphatidic acid acyltransferase, beta) (AGPAT2, Accession XM\_038030). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGPAT2. Ectonucleoside Triphosphate Diphosphohydrolase 3 (ENTPD3, Accession NM\_001248) is another VGAM1741 host target gene. ENTPD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENTPD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENTPD3 BINDING SITE, designated SEQ ID:6922, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ

ID:4452.

[58501] Another function of VGAM1741 is therefore inhibition of Ectonucleoside Triphosphate Diphosphohydrolase 3 (ENTPD3, Accession NM\_001248). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENTPD3. Microtubule-associated Protein, RP/EB Family, Member 2 (MAPRE2, Accession NM\_014268) is another VGAM1741 host target gene. MAPRE2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPRE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE2 BINDING SITE, designated SEQ ID:15548, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58502] Another function of VGAM1741 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 2 (MAPRE2, Accession NM\_014268), a gene which The functional inactivation of the APC gene product is a key event in colorectal tumorigenesis. Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MAPRE2. The function of MAPRE2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Syntrophin, Beta 2 (dystrophin-associated protein A1, 59kDa, basic component 2) (SNTB2, Accession NM\_130845) is another VGAM1741 host target gene. SNTB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNTB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNTB2 BINDING SITE, designated SEQ ID:28379, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58503] Another function of VGAM1741 is therefore inhibition of Syntrophin, Beta 2 (dystrophin-associated protein A1, 59kDa, basic component 2) (SNTB2, Accession NM\_130845). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNTB2. Ankyrin Repeat and SOCS Box-containing 13 (ASB13, Accession NM\_024701)

is another VGAM1741 host target gene. ASB13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ASB13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASB13 BINDING SITE, designated SEQ ID:24013, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58504] Another function of VGAM1741 is therefore inhibition of Ankyrin Repeat and SOCS Box-containing 13 (ASB13, Accession NM\_024701). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASB13. Baculoviral IAP Repeat-containing 1 (BIRC1, Accession NM\_004536) is another VGAM1741 host target gene. BIRC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BIRC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIRC1 BINDING SITE, designated SEQ ID:10887, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA,

also designated SEQ ID:4452.

[58505] Another function of VGAM1741 is therefore inhibition of Baculoviral IAP Repeat-containing 1 (BIRC1, Accession NM\_004536). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC1. CLIPR-59 (Accession NM\_015526) is another VGAM1741 host target gene. CLIPR-59 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLIPR-59, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIPR-59 BINDING SITE, designated SEQ ID:17787, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58506] Another function of VGAM1741 is therefore inhibition of CLIPR-59 (Accession NM\_015526). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIPR-59. KIAA1084 (Accession NM\_014910) is another VGAM1741 host target gene. KIAA1084 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1084 BINDING SITE, designated SEQ ID:17135, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58507] Another function of VGAM1741 is therefore inhibition of KIAA1084 (Accession NM\_014910). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1084. OBTP (Accession NM\_017601) is another VGAM1741 host target gene. OBTP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OBTP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OBTP BINDING SITE, designated SEQ ID:19082, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58508] Another function of VGAM1741 is therefore inhibition of OBTP (Accession NM\_017601). Accordingly, utilities of

VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OBTP. Rpo1-2 (Accession NM\_032212) is another VGAM1741 host target gene. Rpo1-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Rpo1-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rpo1-2 BINDING SITE, designated SEQ ID:25932, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58509] Another function of VGAM1741 is therefore inhibition of Rpo1-2 (Accession NM\_032212). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rpo1-2. SPBPBP (Accession NM\_006692) is another VGAM1741 host target gene. SPBPBP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SPBPBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPBPBP BIND-

ING SITE, designated SEQ ID:13509, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58510] Another function of VGAM1741 is therefore inhibition of SPBPBP (Accession NM\_006692). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPBPBP. Testis-specific Transcript, Y-linked 9 (TTY9, Accession NM\_031927) is another VGAM1741 host target gene. TTY9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TTY9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTY9 BINDING SITE, designated SEQ ID:25678, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58511] Another function of VGAM1741 is therefore inhibition of Testis-specific Transcript, Y-linked 9 (TTY9, Accession NM\_031927). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTY9. LOC145216



(Accession XM\_096730) is another VGAM1741 host target gene. LOC145216 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145216, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145216 BINDING SITE, designated SEQ ID:40505, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58512] Another function of VGAM1741 is therefore inhibition of LOC145216 (Accession XM\_096730). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145216. LOC152457 (Accession XM\_087476) is another VGAM1741 host target gene. LOC152457 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152457, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152457 BINDING SITE, designated SEQ ID:39279, to the nucleotide sequence of VGAM1741 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4452.

[58513] Another function of VGAM1741 is therefore inhibition of LOC152457 (Accession XM\_087476). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152457. LOC221421 (Accession XM\_166428) is another VGAM1741 host target gene. LOC221421 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221421, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221421 BINDING SITE, designated SEQ ID:44323, to the nucleotide sequence of VGAM1741 RNA, herein designated VGAM RNA, also designated SEQ ID:4452.

[58514] Another function of VGAM1741 is therefore inhibition of LOC221421 (Accession XM\_166428). Accordingly, utilities of VGAM1741 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221421. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1742 (VGAM1742) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58515] VGAM1742 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1742 was detected is described hereinabove with reference to Figs. 1–8.

[58516] VGAM1742 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1742 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58517] VGAM1742 gene encodes a VGAM1742 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1742 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1742 precursor RNA is designated SEQ ID:1728, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1728 is located at position 40735 relative to the genome of Cercopithecine Herpesvirus 7.

[58518] VGAM1742 precursor RNA folds onto itself, forming

VGAM1742 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58519] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1742 folded precursor RNA into VGAM1742 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1742 RNA is designated SEQ ID:4453, and is provided hereinbelow with reference to the sequence listing part.

[58520] VGAM1742 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1742 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1742 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58521] VGAM1742 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1742 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1742 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1742 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1742 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58522] The complementary binding of VGAM1742 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1742 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1742 host target RNA into VGAM1742 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58523] It is appreciated that VGAM1742 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1742 host target genes. The mRNA of each one of this plurality of VGAM1742 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1742 RNA, herein designated VGAM RNA, and which when bound by VGAM1742 RNA causes inhibition of translation of respective one or more VGAM1742 host target proteins.

[58524] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1742 gene, herein designated VGAM GENE, on one or more VGAM1742 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58525] It is yet further appreciated that a function of VGAM1742 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1742 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1742 correlate with, and may be deduced from, the identity of the host target genes which VGAM1742 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58526] Nucleotide sequences of the VGAM1742 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1742 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1742 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1742 are further described hereinbelow with reference to Table 1.

[58527] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1742 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1742 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58528] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1742 gene, herein designated VGAM is inhibition of expression of VGAM1742 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1742 correlate with, and may be deduced from, the identity of the target genes which VGAM1742 binds and inhibits, and the function of these target genes,



as elaborated hereinbelow.

[58529] COX10 Homolog, Cytochrome C Oxidase Assembly Protein, Heme A: Farnesyltransferase (yeast) (COX10, Accession NM\_001303) is a VGAM1742 host target gene. COX10 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by COX10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX10 BINDING SITE, designated SEQ ID:6980, to the nucleotide sequence of VGAM1742 RNA, herein designated VGAM RNA, also designated SEQ ID:4453.

[58530] A function of VGAM1742 is therefore inhibition of COX10 Homolog, Cytochrome C Oxidase Assembly Protein, Heme A: Farnesyltransferase (yeast) (COX10, Accession NM\_001303). Accordingly, utilities of VGAM1742 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX10. FLJ22055 (Accession NM\_024779) is another VGAM1742 host target gene. FLJ22055 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ22055, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22055 BINDING SITE, designated SEQ ID:24147, to the nucleotide sequence of VGAM1742 RNA, herein designated VGAM RNA, also designated SEQ ID:4453.

[58531] Another function of VGAM1742 is therefore inhibition of FLJ22055 (Accession NM\_024779). Accordingly, utilities of VGAM1742 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22055. KIAA0802 (Accession XM\_031357) is another VGAM1742 host target gene. KIAA0802 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0802, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0802 BINDING SITE, designated SEQ ID:31352, to the nucleotide sequence of VGAM1742 RNA, herein designated VGAM RNA, also designated SEQ ID:4453.

[58532] Another function of VGAM1742 is therefore inhibition of KIAA0802 (Accession XM\_031357). Accordingly, utilities of VGAM1742 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0802. LOC115574 (Accession XM\_056240) is another VGAM1742 host target gene. LOC115574 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC115574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115574 BINDING SITE, designated SEQ ID:36367, to the nucleotide sequence of VGAM1742 RNA, herein designated VGAM RNA, also designated SEQ ID:4453.

[58533] Another function of VGAM1742 is therefore inhibition of LOC115574 (Accession XM\_056240). Accordingly, utilities of VGAM1742 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115574. LOC221968 (Accession XM\_166524) is another VGAM1742 host target gene. LOC221968 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221968, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221968 BINDING SITE, designated SEQ ID:44471, to

the nucleotide sequence of VGAM1742 RNA, herein designated VGAM RNA, also designated SEQ ID:4453.

[58534] Another function of VGAM1742 is therefore inhibition of LOC221968 (Accession XM\_166524). Accordingly, utilities of VGAM1742 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221968. LOC256021 (Accession XM\_172884) is another VGAM1742 host target gene. LOC256021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256021 BINDING SITE, designated SEQ ID:46164, to the nucleotide sequence of VGAM1742 RNA, herein designated VGAM RNA, also designated SEQ ID:4453.

[58535] Another function of VGAM1742 is therefore inhibition of LOC256021 (Accession XM\_172884). Accordingly, utilities of VGAM1742 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256021. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1743 (VGAM1743) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58536] VGAM1743 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1743 was detected is described hereinabove with reference to Figs. 1–8.

[58537] VGAM1743 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1743 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58538] VGAM1743 gene encodes a VGAM1743 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1743 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1743 precursor RNA is designated SEQ ID:1729, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1729 is located at position 41519 relative to the genome of Cercopithecine Herpesvirus 7.

[58539] VGAM1743 precursor RNA folds onto itself, forming VGAM1743 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58540] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1743 folded precursor RNA into VGAM1743 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 78%) nucleotide sequence of VGAM1743 RNA is designated SEQ ID:4454, and is provided hereinbelow with reference to the sequence listing part.

[58541] VGAM1743 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1743 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1743 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[58542] VGAM1743 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1743 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1743 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1743 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1743 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58543] The complementary binding of VGAM1743 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1743 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1743 host target RNA into VGAM1743 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58544] It is appreciated that VGAM1743 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1743 host target genes. The mRNA of each one of this plurality of VGAM1743 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1743 RNA, herein designated VGAM RNA, and which when bound by VGAM1743 RNA causes inhibition of translation of respective one or more VGAM1743 host target proteins.

[58545] It is further appreciated by one skilled in the art that the



mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1743 gene, herein designated VGAM GENE, on one or more VGAM1743 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58546] It is yet further appreciated that a function of VGAM1743 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1743 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1743 correlate with, and may be deduced from, the

identity of the host target genes which VGAM1743 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58547] Nucleotide sequences of the VGAM1743 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1743 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1743 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1743 are further described hereinbelow with reference to Table 1.

[58548] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1743 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1743 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58549] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1743 gene, herein designated VGAM is inhibition of expression of VGAM1743 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1743 correlate with, and may be deduced from, the identity of the target genes which VGAM1743

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58550] A Disintegrin and Metalloproteinase Domain 19 (meltrin beta) (ADAM19, Accession NM\_033274) is a VGAM1743 host target gene. ADAM19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAM19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM19 BINDING SITE, designated SEQ ID:27097, to the nucleotide sequence of VGAM1743 RNA, herein designated VGAM RNA, also designated SEQ ID:4454.

[58551] A function of VGAM1743 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 19 (meltrin beta) (ADAM19, Accession NM\_033274), a gene which participates in the proteolytic processing of beta-type neuregulin isoforms . Accordingly, utilities of VGAM1743 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM19. The function of ADAM19 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM179.Nuclear Mitotic Apparatus Protein 1 (NUMA1, Accession XM\_167853) is another VGAM1743 host target gene. NUMA1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NUMA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUMA1 BINDING SITE, designated SEQ ID:44879, to the nucleotide sequence of VGAM1743 RNA, herein designated VGAM RNA, also designated SEQ ID:4454.

[58552] Another function of VGAM1743 is therefore inhibition of Nuclear Mitotic Apparatus Protein 1 (NUMA1, Accession XM\_167853), a gene which is nuclear mitotic apparatus protein. Accordingly, utilities of VGAM1743 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUMA1. The function of NUMA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM192.ATIP1 (Accession NM\_020749) is another VGAM1743 host target gene. ATIP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by ATIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATIP1 BINDING SITE, designated SEQ ID:21861, to the nucleotide sequence of VGAM1743 RNA, herein designated VGAM RNA, also designated SEQ ID:4454.

[58553] Another function of VGAM1743 is therefore inhibition of ATIP1 (Accession NM\_020749). Accordingly, utilities of VGAM1743 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATIP1. KIAA0295 (Accession XM\_042833) is another VGAM1743 host target gene. KIAA0295 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0295 BINDING SITE, designated SEQ ID:33783, to the nucleotide sequence of VGAM1743 RNA, herein designated VGAM RNA, also designated SEQ ID:4454.

[58554] Another function of VGAM1743 is therefore inhibition of KIAA0295 (Accession XM\_042833). Accordingly, utilities

of VGAM1743 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0295. Ring Finger Protein 24 (RNF24, Accession NM\_007219) is another VGAM1743 host target gene. RNF24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF24 BINDING SITE, designated SEQ ID:14084, to the nucleotide sequence of VGAM1743 RNA, herein designated VGAM RNA, also designated SEQ ID:4454.

[58555] Another function of VGAM1743 is therefore inhibition of Ring Finger Protein 24 (RNF24, Accession NM\_007219). Accordingly, utilities of VGAM1743 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF24. VIT1 (Accession NM\_018693) is another VGAM1743 host target gene. VIT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by VIT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of VIT1 BINDING SITE, designated SEQ ID:20766, to the nucleotide sequence of VGAM1743 RNA, herein designated VGAM RNA, also designated SEQ ID:4454.

[58556] Another function of VGAM1743 is therefore inhibition of VIT1 (Accession NM\_018693). Accordingly, utilities of VGAM1743 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIT1. LOC118786 (Accession XM\_061147) is another VGAM1743 host target gene. LOC118786 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC118786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118786 BINDING SITE, designated SEQ ID:37197, to the nucleotide sequence of VGAM1743 RNA, herein designated VGAM RNA, also designated SEQ ID:4454.

[58557] Another function of VGAM1743 is therefore inhibition of LOC118786 (Accession XM\_061147). Accordingly, utilities of VGAM1743 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118786. LOC121441 (Accession XM\_058561) is an-

other VGAM1743 host target gene. LOC121441 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC121441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121441 BINDING SITE, designated SEQ ID:36659, to the nucleotide sequence of VGAM1743 RNA, herein designated VGAM RNA, also designated SEQ ID:4454.

[58558] Another function of VGAM1743 is therefore inhibition of LOC121441 (Accession XM\_058561). Accordingly, utilities of VGAM1743 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121441. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1744 (VGAM1744) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58559] VGAM1744 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1744 was detected is de-



scribed hereinabove with reference to Figs. 1–8.

[58560] VGAM1744 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1744 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58561] VGAM1744 gene encodes a VGAM1744 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1744 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1744 precursor RNA is designated SEQ ID:1730, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1730 is located at position 38434 relative to the genome of Cercopithecine Herpesvirus 7.

[58562] VGAM1744 precursor RNA folds onto itself, forming VGAM1744 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58563] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1744 folded precursor RNA into VGAM1744 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1744 RNA is designated SEQ ID:4455, and is provided hereinbelow with reference to the sequence listing part.

[58564] VGAM1744 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1744 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1744 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58565] VGAM1744 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1744 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1744 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1744 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1744 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58566] The complementary binding of VGAM1744 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1744 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1744 host target RNA into VGAM1744 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58567] It is appreciated that VGAM1744 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1744 host target genes. The mRNA of each one of this plurality of VGAM1744 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1744 RNA, herein designated VGAM RNA, and which when bound by VGAM1744 RNA causes inhibition of translation of respective one or more VGAM1744 host target proteins.

[58568] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1744 gene, herein designated VGAM GENE, on one or more VGAM1744 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58569] It is yet further appreciated that a function of VGAM1744 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1744 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1744 correlate with, and may be deduced from, the identity of the host target genes which VGAM1744 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58570] Nucleotide sequences of the VGAM1744 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1744 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1744 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1744 are further described hereinbelow with reference to Table 1.

[58571] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1744 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1744 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58572] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1744 gene, herein designated VGAM is inhibition of expression of VGAM1744 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1744 correlate with, and may be deduced from, the identity of the target genes which VGAM1744 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58573] ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 5 (ABCC5, Accession NM\_005688) is a VGAM1744 host target gene. ABCC5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCC5, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC5 BINDING SITE, designated SEQ ID:12249, to the nucleotide sequence of VGAM1744 RNA, herein designated VGAM RNA, also designated SEQ ID:4455.

[58574] A function of VGAM1744 is therefore inhibition of ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 5 (ABCC5, Accession NM\_005688), a gene which acts as a multispecific organic anion pump which can transport nucleotide analogs. Accordingly, utilities of VGAM1744 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC5. The function of ABCC5 has been established by previous studies. Multidrug resistance (MDR) proteins (MRPs) mediate the extrusion of drugs from normal cells and tumors. MDR/ATP-binding cassette (ABC) membrane proteins are involved in energy-dependent transport of a wide variety of substrates. Allikmets et al. (1996) and Kool et al. (1997) used EST database searching to identify partial cDNAs encoding ABCC5 (see OMIM Ref. No. ABCC4, 605250). Using RT-PCR with degenerate primers, Suzuki et al. (1997) isolated a cDNA encoding short MRP, an apparent splice vari-

ant of ABCC5 (Suzuki et al., 2000). By EST database searching, followed by 5-prime RACE, Belinsky et al. (1998) obtained a cDNA encoding full-length ABCC5, which they termed MOATC (multispecific organic anion transporter C). Sequence analysis predicted that the 1,437-amino acid protein, like other ABC transporters, contains Walker A, B and C motifs, nucleotide-binding folds, and 12 transmembrane spanning helices in 2 hydrophobic domains. Kool et al. (1997), Suzuki et al. (1997), and Belinsky et al. (1998) performed Northern blot analysis which revealed ubiquitous expression of a 6.6-kb ABCC5 transcript with highest levels in skeletal muscle followed by brain, kidney, testis, and heart. Oguri et al. (2000) noted that the effectiveness of platinum drugs in lung cancer is limited by the development of drug resistance to them. Quantitative RT-PCR analysis showed that expression of ABCC5, like that of ABCC1 (OMIM Ref. No. 158343) and gamma-glutamylcysteine synthetase (see OMIM Ref. No. 606857), is increased in normal and tumor lung tissue from patients with previous platinum exposure. However, in vitro exposure of lung cancer cells to the platinum drug cisplatin, or of mononuclear cells to carboplatin, does not cause increased expression of



ABCC5.

[58575] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58576] Suzuki, T.; Sasaki, H.; Kuh, H.-J.; Agui, M.; Tatsumi, Y.; Tanabe, S.; Terada, M.; Saijo, N.; Nishio, K. : Detailed structural analysis on both human MRP5 and mouse mrp5 transcripts. Gene 242: 167–173, 2000. ; and

[58577] Oguri, T.; Isobe, T.; Suzuki, T.; Nishio, K.; Fujiwara, Y.; Kato, O.; Yamakido, M. : Increased expression of the MRP5 gene is associated with exposure to platinum drugs in lung cancer.

[58578] Further studies establishing the function and utilities of ABCC5 are found in John Hopkins OMIM database record ID 605251, and in cited publications numbered 282 and 5013–4401 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ21736 (Accession NM\_024922) is another VGAM1744 host target gene. FLJ21736 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21736, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of FLJ21736 BINDING SITE, designated SEQ ID:24460, to the nucleotide sequence of VGAM1744 RNA, herein designated VGAM RNA, also designated SEQ ID:4455.

[58579] Another function of VGAM1744 is therefore inhibition of FLJ21736 (Accession NM\_024922). Accordingly, utilities of VGAM1744 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21736. G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM\_139201) is another VGAM1744 host target gene. GIT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GIT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT2 BINDING SITE, designated SEQ ID:29213, to the nucleotide sequence of VGAM1744 RNA, herein designated VGAM RNA, also designated SEQ ID:4455.

[58580] Another function of VGAM1744 is therefore inhibition of G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM\_139201). Accordingly, utilities of VGAM1744 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with GIT2. KIAA1128 (Accession XM\_043596) is another VGAM1744 host target gene. KIAA1128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1128 BINDING SITE, designated SEQ ID:33968, to the nucleotide sequence of VGAM1744 RNA, herein designated VGAM RNA, also designated SEQ ID:4455.

[58581] Another function of VGAM1744 is therefore inhibition of KIAA1128 (Accession XM\_043596). Accordingly, utilities of VGAM1744 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1128. KIAA1384 (Accession XM\_035405) is another VGAM1744 host target gene. KIAA1384 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1384, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1384 BINDING SITE, designated SEQ ID:32260, to the

nucleotide sequence of VGAM1744 RNA, herein designated VGAM RNA, also designated SEQ ID:4455.

[58582] Another function of VGAM1744 is therefore inhibition of KIAA1384 (Accession XM\_035405). Accordingly, utilities of VGAM1744 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1384. KIAA1958 (Accession XM\_088566) is another VGAM1744 host target gene. KIAA1958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1958 BINDING SITE, designated SEQ ID:39831, to the nucleotide sequence of VGAM1744 RNA, herein designated VGAM RNA, also designated SEQ ID:4455.

[58583] Another function of VGAM1744 is therefore inhibition of KIAA1958 (Accession XM\_088566). Accordingly, utilities of VGAM1744 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1958. LOC143915 (Accession XM\_096502) is another VGAM1744 host target gene. LOC143915 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC143915, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143915 BINDING SITE, designated SEQ ID:40378, to the nucleotide sequence of VGAM1744 RNA, herein designated VGAM RNA, also designated SEQ ID:4455.

[58584] Another function of VGAM1744 is therefore inhibition of LOC143915 (Accession XM\_096502). Accordingly, utilities of VGAM1744 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143915. LOC200558 (Accession XM\_114258) is another VGAM1744 host target gene. LOC200558 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200558 BINDING SITE, designated SEQ ID:42819, to the nucleotide sequence of VGAM1744 RNA, herein designated VGAM RNA, also designated SEQ ID:4455.

[58585] Another function of VGAM1744 is therefore inhibition of LOC200558 (Accession XM\_114258). Accordingly, utilities

of VGAM1744 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200558. LOC202934 (Accession XM\_117486) is another VGAM1744 host target gene. LOC202934 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202934 BINDING SITE, designated SEQ ID:43455, to the nucleotide sequence of VGAM1744 RNA, herein designated VGAM RNA, also designated SEQ ID:4455.

[58586] Another function of VGAM1744 is therefore inhibition of LOC202934 (Accession XM\_117486). Accordingly, utilities of VGAM1744 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202934. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1745 (VGAM1745) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58587] VGAM1745 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1745 was detected is described hereinabove with reference to Figs. 1–8.

[58588] VGAM1745 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1745 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58589] VGAM1745 gene encodes a VGAM1745 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1745 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1745 precursor RNA is designated SEQ ID:1731, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1731 is located at position 37836 relative to the genome of Cercopithecine Herpesvirus 7.

[58590] VGAM1745 precursor RNA folds onto itself, forming VGAM1745 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58591] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1745 folded precursor RNA into VGAM1745 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1745 RNA is designated SEQ ID:4456, and is provided hereinbelow with reference to the sequence listing part.

[58592] VGAM1745 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1745 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1745 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated



5`UTR, PROTEIN CODING and 3`UTR respectively.

[58593] VGAM1745 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1745 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1745 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1745 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1745 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58594] The complementary binding of VGAM1745 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1745 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1745 host target RNA into VGAM1745 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58595] It is appreciated that VGAM1745 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1745 host target genes. The mRNA of each one of this plurality of VGAM1745 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1745 RNA, herein designated VGAM RNA, and which when bound by VGAM1745 RNA causes inhibition of translation of respective one or more VGAM1745 host target proteins.

[58596] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1745 gene, herein designated VGAM GENE, on one or more VGAM1745 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58597] It is yet further appreciated that a function of VGAM1745 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1745 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1745 correlate with, and may be deduced from, the identity of the host target genes which VGAM1745 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58598] Nucleotide sequences of the VGAM1745 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1745 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1745 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1745 are further  
described hereinbelow with reference to Table 1.

[58599] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1745 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1745 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[58600] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1745 gene, herein designated VGAM is  
inhibition of expression of VGAM1745 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1745 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1745  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[58601] Protein Kinase C, Nu (PRKCN, Accession NM\_005813) is a  
VGAM1745 host target gene. PRKCN BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKCN BINDING SITE, designated SEQ ID:12397, to the nucleotide sequence of VGAM1745 RNA, herein designated VGAM RNA, also designated SEQ ID:4456.

[58602] A function of VGAM1745 is therefore inhibition of Protein Kinase C,  $\alpha$  (PRKCN, Accession NM\_005813). Accordingly, utilities of VGAM1745 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKCN. KIAA1432 (Accession XM\_039698) is another VGAM1745 host target gene. KIAA1432 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1432 BINDING SITE, designated SEQ ID:33147, to the nucleotide sequence of VGAM1745 RNA, herein designated VGAM RNA, also designated SEQ ID:4456.

[58603] Another function of VGAM1745 is therefore inhibition of

KIAA1432 (Accession XM\_039698). Accordingly, utilities of VGAM1745 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1432. MO25 (Accession NM\_016289) is another VGAM1745 host target gene. MO25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MO25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MO25 BINDING SITE, designated SEQ ID:18414, to the nucleotide sequence of VGAM1745 RNA, herein designated VGAM RNA, also designated SEQ ID:4456.

[58604] Another function of VGAM1745 is therefore inhibition of MO25 (Accession NM\_016289). Accordingly, utilities of VGAM1745 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MO25. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1746 (VGAM1746) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58605] VGAM1746 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1746 was detected is described hereinabove with reference to Figs. 1–8.

[58606] VGAM1746 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1746 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58607] VGAM1746 gene encodes a VGAM1746 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1746 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1746 precursor RNA is designated SEQ ID:1732, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1732 is located at position 40845 relative to the genome of Cercopithecine Herpesvirus 7.

[58608] VGAM1746 precursor RNA folds onto itself, forming VGAM1746 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58609] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1746 folded precursor RNA into VGAM1746 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1746 RNA is designated SEQ ID:4457, and is provided hereinbelow with reference to the sequence listing part.

[58610] VGAM1746 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1746 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1746 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated



5`UTR, PROTEIN CODING and 3`UTR respectively.

[58611] VGAM1746 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1746 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1746 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1746 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1746 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58612] The complementary binding of VGAM1746 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1746 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1746 host target RNA into VGAM1746 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58613] It is appreciated that VGAM1746 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1746 host target genes. The mRNA of each one of this plurality of VGAM1746 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1746 RNA, herein designated VGAM RNA, and which when bound by VGAM1746 RNA causes inhibition of translation of respective one or more VGAM1746 host target proteins.

[58614] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1746 gene, herein designated VGAM GENE, on one or more VGAM1746 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58615] It is yet further appreciated that a function of VGAM1746 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1746 correlate with, and may be deduced from, the identity of the host target genes which VGAM1746 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58616] Nucleotide sequences of the VGAM1746 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1746 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1746 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1746 are further  
described hereinbelow with reference to Table 1.

[58617] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1746 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1746 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[58618] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1746 gene, herein designated VGAM is  
inhibition of expression of VGAM1746 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1746 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1746  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[58619] SNL (Accession NM\_003088) is a VGAM1746 host target  
gene. SNL BINDING SITE is HOST TARGET binding site

found in the 3` untranslated region of mRNA encoded by SNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNL BINDING SITE, designated SEQ ID:9062, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58620] A function of VGAM1746 is therefore inhibition of SNL (Accession NM\_003088), a gene which organizes filamentous actin into bundles with a minimum of 4.1:1 actin/fascin ratio. Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNL. The function of SNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675.Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM\_003242) is another VGAM1746 host target gene. TGFB2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TGFB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of TGFBR2 BINDING SITE, designated SEQ ID:9236, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58621] Another function of VGAM1746 is therefore inhibition of Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFBR2, Accession NM\_003242). Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFBR2. Thiamin Pyrophosphokinase 1 (TPK1, Accession NM\_022445) is another VGAM1746 host target gene. TPK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TPK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPK1 BINDING SITE, designated SEQ ID:22778, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58622] Another function of VGAM1746 is therefore inhibition of Thiamin Pyrophosphokinase 1 (TPK1, Accession NM\_022445), a gene which catalyzes the conversion of thiamine, a form of vitamin B1, to thiamine pyrophos-

phate . Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPK1. The function of TPK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM475.KIAA0528 (Accession XM\_051454) is another VGAM1746 host target gene. KIAA0528 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0528, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0528 BINDING SITE, designated SEQ ID:35839, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58623] Another function of VGAM1746 is therefore inhibition of KIAA0528 (Accession XM\_051454). Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0528. KIAA1128 (Accession XM\_043596) is another VGAM1746 host target gene. KIAA1128 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by KIAA1128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1128 BINDING SITE, designated SEQ ID:33963, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58624] Another function of VGAM1746 is therefore inhibition of KIAA1128 (Accession XM\_043596). Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1128. Zinc Finger Protein 387 (ZNF387, Accession NM\_014682) is another VGAM1746 host target gene. ZNF387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF387 BINDING SITE, designated SEQ ID:16176, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58625] Another function of VGAM1746 is therefore inhibition of



Zinc Finger Protein 387 (ZNF387, Accession NM\_014682). Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF387. LOC197317 (Accession XM\_117014) is another VGAM1746 host target gene. LOC197317 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC197317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197317 BINDING SITE, designated SEQ ID:43205, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58626] Another function of VGAM1746 is therefore inhibition of LOC197317 (Accession XM\_117014). Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197317. LOC199926 (Accession XM\_117157) is another VGAM1746 host target gene. LOC199926 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC199926, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199926 BINDING SITE, designated SEQ ID:43259, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58627] Another function of VGAM1746 is therefore inhibition of LOC199926 (Accession XM\_117157). Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199926. LOC202025 (Accession XM\_117353) is another VGAM1746 host target gene. LOC202025 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202025 BINDING SITE, designated SEQ ID:43403, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58628] Another function of VGAM1746 is therefore inhibition of LOC202025 (Accession XM\_117353). Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC202025. LOC202316 (Accession XM\_117380) is another VGAM1746 host target gene. LOC202316 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202316, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202316 BINDING SITE, designated SEQ ID:43423, to the nucleotide sequence of VGAM1746 RNA, herein designated VGAM RNA, also designated SEQ ID:4457.

[58629] Another function of VGAM1746 is therefore inhibition of LOC202316 (Accession XM\_117380). Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202316. LOC90494 (Accession XM\_032161) is another VGAM1746 host target gene. LOC90494 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90494 BINDING SITE, designated SEQ ID:31577, to the nucleotide sequence of VGAM1746 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4457.

[58630] Another function of VGAM1746 is therefore inhibition of LOC90494 (Accession XM\_032161). Accordingly, utilities of VGAM1746 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90494. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1747 (VGAM1747) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58631] VGAM1747 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1747 was detected is described hereinabove with reference to Figs. 1–8.

[58632] VGAM1747 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1747 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58633] VGAM1747 gene encodes a VGAM1747 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1747 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1747 precursor RNA is designated SEQ ID:1733, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1733 is located at position 11942 relative to the genome of Camelpox Virus.

[58634] VGAM1747 precursor RNA folds onto itself, forming VGAM1747 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58635] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1747 folded precursor RNA into VGAM1747 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM1747 RNA is designated SEQ ID:4458, and is provided hereinbelow with reference to the sequence listing part.

[58636] VGAM1747 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1747 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1747 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58637] VGAM1747 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1747 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1747 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1747 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1747 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[58638] The complementary binding of VGAM1747 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1747 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1747 host target RNA into VGAM1747 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58639] It is appreciated that VGAM1747 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1747 host target genes. The mRNA of

each one of this plurality of VGAM1747 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1747 RNA, herein designated VGAM RNA, and which when bound by VGAM1747 RNA causes inhibition of translation of respective one or more VGAM1747 host target proteins.

[58640] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1747 gene, herein designated VGAM GENE, on one or more VGAM1747 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science



294,779 (2001)).

[58641] It is yet further appreciated that a function of VGAM1747 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1747 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1747 correlate with, and may be deduced from, the identity of the host target genes which VGAM1747 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58642] Nucleotide sequences of the VGAM1747 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1747 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1747 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1747 are further described hereinbelow with reference to Table 1.

[58643] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1747 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1747 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58644] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1747 gene, herein designated VGAM is inhibition of expression of VGAM1747 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1747 correlate with, and may be deduced from, the identity of the target genes which VGAM1747 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58645] MGC4342 (Accession NM\_024329) is a VGAM1747 host target gene. MGC4342 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4342 BINDING SITE, designated SEQ ID:23623, to the nucleotide sequence of VGAM1747 RNA, herein designated VGAM RNA, also designated SEQ ID:4458.

[58646] A function of VGAM1747 is therefore inhibition of MGC4342 (Accession NM\_024329). Accordingly, utilities of VGAM1747 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC4342. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1748 (VGAM1748) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58647] VGAM1748 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1748 was detected is described hereinabove with reference to Figs. 1–8.

[58648] VGAM1748 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1748 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58649] VGAM1748 gene encodes a VGAM1748 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1748 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1748 precursor RNA is desig-

nated SEQ ID:1734, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1734 is located at position 67 relative to the genome of Camelpox Virus.

- [58650] VGAM1748 precursor RNA folds onto itself, forming VGAM1748 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [58651] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1748 folded precursor RNA into VGAM1748 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1748 RNA is designated SEQ ID:4459, and is provided hereinbelow with reference to the sequence

listing part.

[58652] VGAM1748 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1748 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1748 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58653] VGAM1748 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1748 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1748 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1748 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1748 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58654] The complementary binding of VGAM1748 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1748 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1748 host target RNA into VGAM1748 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58655] It is appreciated that VGAM1748 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1748 host target genes. The mRNA of each one of this plurality of VGAM1748 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1748 RNA, herein designated VGAM

RNA, and which when bound by VGAM1748 RNA causes inhibition of translation of respective one or more VGAM1748 host target proteins.

[58656] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1748 gene, herein designated VGAM GENE, on one or more VGAM1748 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58657] It is yet further appreciated that a function of VGAM1748 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1748 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1748 correlate with, and may be deduced from, the identity of the host target genes which VGAM1748 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58658] Nucleotide sequences of the VGAM1748 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1748 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1748 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1748 are further described hereinbelow with reference to Table 1.

[58659] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1748 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1748 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58660] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1748 gene, herein designated VGAM is



inhibition of expression of VGAM1748 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1748 correlate with, and may be deduced from, the identity of the target genes which VGAM1748 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58661] FLJ11210 (Accession XM\_005298) is a VGAM1748 host target gene. FLJ11210 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11210 BINDING SITE, designated SEQ ID:29971, to the nucleotide sequence of VGAM1748 RNA, herein designated VGAM RNA, also designated SEQ ID:4459.

[58662] A function of VGAM1748 is therefore inhibition of FLJ11210 (Accession XM\_005298). Accordingly, utilities of VGAM1748 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11210. HTCD37 (Accession XM\_041884) is another VGAM1748 host target gene. HTCD37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by HTCD37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTCD37 BINDING SITE, designated SEQ ID:33618, to the nucleotide sequence of VGAM1748 RNA, herein designated VGAM RNA, also designated SEQ ID:4459.

[58663] Another function of VGAM1748 is therefore inhibition of HTCD37 (Accession XM\_041884). Accordingly, utilities of VGAM1748 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTCD37. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1749 (VGAM1749) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58664] VGAM1749 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1749 was detected is described hereinabove with reference to Figs. 1-8.

[58665] VGAM1749 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Camelpox Virus.

VGAM1749 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58666] VGAM1749 gene encodes a VGAM1749 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1749 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1749 precursor RNA is designated SEQ ID:1735, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1735 is located at position 4361 relative to the genome of Camelpox Virus.

[58667] VGAM1749 precursor RNA folds onto itself, forming VGAM1749 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58668] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1749 folded precursor RNA into VGAM1749 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1749 RNA is designated SEQ ID:4460, and is provided hereinbelow with reference to the sequence listing part.

[58669] VGAM1749 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1749 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1749 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58670] VGAM1749 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1749 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1749 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1749 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1749 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58671] The complementary binding of VGAM1749 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1749 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1749

host target RNA into VGAM1749 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58672] It is appreciated that VGAM1749 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1749 host target genes. The mRNA of each one of this plurality of VGAM1749 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1749 RNA, herein designated VGAM RNA, and which when bound by VGAM1749 RNA causes inhibition of translation of respective one or more VGAM1749 host target proteins.

[58673] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1749 gene, herein designated VGAM GENE, on one or more VGAM1749 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58674] It is yet further appreciated that a function of VGAM1749 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1749 correlate with, and may be deduced from, the identity of the host target genes which VGAM1749 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58675] Nucleotide sequences of the VGAM1749 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1749 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1749 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1749 are further

described hereinbelow with reference to Table 1.

[58676] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1749 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1749 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58677] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1749 gene, herein designated VGAM is inhibition of expression of VGAM1749 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1749 correlate with, and may be deduced from, the identity of the target genes which VGAM1749 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58678] FLJ13614 (Accession NM\_139076) is a VGAM1749 host target gene. FLJ13614 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13614, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13614 BINDING SITE,



designated SEQ ID:29148, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58679] A function of VGAM1749 is therefore inhibition of FLJ13614 (Accession NM\_139076). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13614. FLJ20508 (Accession NM\_017850) is another VGAM1749 host target gene. FLJ20508 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20508 BINDING SITE, designated SEQ ID:19517, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58680] Another function of VGAM1749 is therefore inhibition of FLJ20508 (Accession NM\_017850). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20508. KIAA1189 (Accession XM\_050508) is another VGAM1749 host target gene. KIAA1189 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1189 BINDING SITE, designated SEQ ID:35650, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58681] Another function of VGAM1749 is therefore inhibition of KIAA1189 (Accession XM\_050508). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1189. MGC10955 (Accession NM\_032676) is another VGAM1749 host target gene. MGC10955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10955 BINDING SITE, designated SEQ ID:26397, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58682] Another function of VGAM1749 is therefore inhibition of

MGC10955 (Accession NM\_032676). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10955. PRO1163 (Accession NM\_018576) is another VGAM1749 host target gene. PRO1163 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1163, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1163 BINDING SITE, designated SEQ ID:20653, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58683] Another function of VGAM1749 is therefore inhibition of PRO1163 (Accession NM\_018576). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1163. LOC118706 (Accession XM\_058336) is another VGAM1749 host target gene. LOC118706 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC118706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC118706 BINDING SITE, designated SEQ ID:36596, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58684] Another function of VGAM1749 is therefore inhibition of LOC118706 (Accession XM\_058336). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118706. LOC143158 (Accession XM\_084445) is another VGAM1749 host target gene. LOC143158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143158 BINDING SITE, designated SEQ ID:37591, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58685] Another function of VGAM1749 is therefore inhibition of LOC143158 (Accession XM\_084445). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143158. LOC150862 (Accession XM\_087029) is an-

other VGAM1749 host target gene. LOC150862 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150862, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150862 BINDING SITE, designated SEQ ID:39016, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58686] Another function of VGAM1749 is therefore inhibition of LOC150862 (Accession XM\_087029). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150862. LOC151826 (Accession XM\_087312) is another VGAM1749 host target gene. LOC151826 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151826 BINDING SITE, designated SEQ ID:39167, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58687] Another function of VGAM1749 is therefore inhibition of LOC151826 (Accession XM\_087312). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151826. LOC158267 (Accession XM\_088528) is another VGAM1749 host target gene. LOC158267 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158267 BINDING SITE, designated SEQ ID:39793, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58688] Another function of VGAM1749 is therefore inhibition of LOC158267 (Accession XM\_088528). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158267. LOC220466 (Accession XM\_058363) is another VGAM1749 host target gene. LOC220466 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220466, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220466 BINDING SITE, designated SEQ ID:36610, to the nucleotide sequence of VGAM1749 RNA, herein designated VGAM RNA, also designated SEQ ID:4460.

[58689] Another function of VGAM1749 is therefore inhibition of LOC220466 (Accession XM\_058363). Accordingly, utilities of VGAM1749 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220466. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1750 (VGAM1750) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58690] VGAM1750 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1750 was detected is described hereinabove with reference to Figs. 1-8.

[58691] VGAM1750 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1750 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[58692] VGAM1750 gene encodes a VGAM1750 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1750 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1750 precursor RNA is designated SEQ ID:1736, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1736 is located at position 1194 relative to the genome of Camelpox Virus.

[58693] VGAM1750 precursor RNA folds onto itself, forming VGAM1750 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58694] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1750 folded precursor RNA into VGAM1750



RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1750 RNA is designated SEQ ID:4461, and is provided hereinbelow with reference to the sequence listing part.

[58695] VGAM1750 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1750 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1750 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58696] VGAM1750 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1750 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1750 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1750 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1750 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58697] The complementary binding of VGAM1750 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1750 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1750 host target RNA into VGAM1750 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[58698] It is appreciated that VGAM1750 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1750 host target genes. The mRNA of each one of this plurality of VGAM1750 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1750 RNA, herein designated VGAM RNA, and which when bound by VGAM1750 RNA causes inhibition of translation of respective one or more VGAM1750 host target proteins.

[58699] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1750 gene, herein designated VGAM GENE, on one or more VGAM1750 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58700] It is yet further appreciated that a function of VGAM1750 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1750 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1750 correlate with, and may be deduced from, the identity of the host target genes which VGAM1750 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58701] Nucleotide sequences of the VGAM1750 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1750 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1750 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1750 are further described hereinbelow with reference to Table 1.

[58702] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1750 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1750 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58703] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1750 gene, herein designated VGAM is inhibition of expression of VGAM1750 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1750 correlate with, and may be deduced from, the identity of the target genes which VGAM1750 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58704] LOC152078 (Accession XM\_087376) is a VGAM1750 host target gene. LOC152078 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152078 BINDING SITE, designated SEQ ID:39213, to the nucleotide sequence of VGAM1750 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4461.

[58705] A function of VGAM1750 is therefore inhibition of LOC152078 (Accession XM\_087376). Accordingly, utilities of VGAM1750 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152078. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1751 (VGAM1751) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58706] VGAM1751 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1751 was detected is described hereinabove with reference to Figs. 1–8.

[58707] VGAM1751 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1751 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58708] VGAM1751 gene encodes a VGAM1751 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1751 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1751 precursor RNA is designated SEQ ID:1737, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1737 is located at position 58 relative to the genome of Camelpox Virus.

- [58709] VGAM1751 precursor RNA folds onto itself, forming VGAM1751 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [58710] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1751 folded precursor RNA into VGAM1751 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1751 RNA is designated SEQ ID:4462, and is provided hereinbelow with reference to the sequence listing part.

[58711] VGAM1751 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1751 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1751 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58712] VGAM1751 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1751 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1751 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and



BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1751 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1751 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58713] The complementary binding of VGAM1751 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1751 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1751 host target RNA into VGAM1751 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58714] It is appreciated that VGAM1751 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1751 host target genes. The mRNA of

each one of this plurality of VGAM1751 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1751 RNA, herein designated VGAM RNA, and which when bound by VGAM1751 RNA causes inhibition of translation of respective one or more VGAM1751 host target proteins.

[58715] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1751 gene, herein designated VGAM GENE, on one or more VGAM1751 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[58716] It is yet further appreciated that a function of VGAM1751 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1751 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1751 correlate with, and may be deduced from, the identity of the host target genes which VGAM1751 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58717] Nucleotide sequences of the VGAM1751 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1751 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1751 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1751 are further described hereinbelow with reference to Table 1.

[58718] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1751 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1751 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58719] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1751 gene, herein designated VGAM is inhibition of expression of VGAM1751 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1751 correlate with, and may be deduced from, the identity of the target genes which VGAM1751 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58720] LOC152078 (Accession XM\_087376) is a VGAM1751 host target gene. LOC152078 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152078 BINDING SITE, designated SEQ ID:39213, to the nucleotide sequence of VGAM1751 RNA, herein designated VGAM RNA, also designated SEQ ID:4462.

[58721] A function of VGAM1751 is therefore inhibition of LOC152078 (Accession XM\_087376). Accordingly, utilities of VGAM1751 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC152078. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1752 (VGAM1752) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58722] VGAM1752 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1752 was detected is described hereinabove with reference to Figs. 1–8.

[58723] VGAM1752 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1752 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58724] VGAM1752 gene encodes a VGAM1752 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1752 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1752 precursor RNA is desig-

nated SEQ ID:1738, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1738 is located at position 2927 relative to the genome of Camelpox Virus.

- [58725] VGAM1752 precursor RNA folds onto itself, forming VGAM1752 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [58726] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1752 folded precursor RNA into VGAM1752 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1752 RNA is designated SEQ ID:4463, and is provided hereinbelow with reference to the sequence

listing part.

[58727] VGAM1752 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1752 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1752 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58728] VGAM1752 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1752 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1752 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1752 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1752 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58729] The complementary binding of VGAM1752 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1752 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1752 host target RNA into VGAM1752 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58730] It is appreciated that VGAM1752 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1752 host target genes. The mRNA of each one of this plurality of VGAM1752 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1752 RNA, herein designated VGAM



RNA, and which when bound by VGAM1752 RNA causes inhibition of translation of respective one or more VGAM1752 host target proteins.

[58731] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1752 gene, herein designated VGAM GENE, on one or more VGAM1752 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58732] It is yet further appreciated that a function of VGAM1752 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1752 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1752 correlate with, and may be deduced from, the identity of the host target genes which VGAM1752 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58733] Nucleotide sequences of the VGAM1752 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1752 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1752 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1752 are further described hereinbelow with reference to Table 1.

[58734] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1752 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1752 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58735] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1752 gene, herein designated VGAM is

inhibition of expression of VGAM1752 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1752 correlate with, and may be deduced from, the identity of the target genes which VGAM1752 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58736] Chromosome 11 Open Reading Frame 23 (C11orf23, Accession NM\_018312) is a VGAM1752 host target gene. C11orf23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C11orf23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf23 BINDING SITE, designated SEQ ID:20298, to the nucleotide sequence of VGAM1752 RNA, herein designated VGAM RNA, also designated SEQ ID:4463.

[58737] A function of VGAM1752 is therefore inhibition of Chromosome 11 Open Reading Frame 23 (C11orf23, Accession NM\_018312). Accordingly, utilities of VGAM1752 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf23. LOC160646 (Accession XM\_090413) is another VGAM1752 host target

gene. LOC160646 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC160646, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160646 BINDING SITE, designated SEQ ID:40000, to the nucleotide sequence of VGAM1752 RNA, herein designated VGAM RNA, also designated SEQ ID:4463.

[58738] Another function of VGAM1752 is therefore inhibition of LOC160646 (Accession XM\_090413). Accordingly, utilities of VGAM1752 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160646. LOC201475 (Accession XM\_113967) is another VGAM1752 host target gene. LOC201475 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201475 BINDING SITE, designated SEQ ID:42576, to the nucleotide sequence of VGAM1752 RNA, herein designated VGAM RNA, also designated SEQ ID:4463.

[58739] Another function of VGAM1752 is therefore inhibition of LOC201475 (Accession XM\_113967). Accordingly, utilities of VGAM1752 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201475. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1753 (VGAM1753) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58740] VGAM1753 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1753 was detected is described hereinabove with reference to Figs. 1–8.

[58741] VGAM1753 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1753 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58742] VGAM1753 gene encodes a VGAM1753 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1753 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1753 precursor RNA is designated SEQ ID:1739, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1739 is located at position 2271 relative to the genome of Camelpox Virus.

[58743] VGAM1753 precursor RNA folds onto itself, forming VGAM1753 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58744] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1753 folded precursor RNA into VGAM1753 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1753 RNA is designated SEQ ID:4464, and is provided hereinbelow with reference to the sequence listing part.

[58745] VGAM1753 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1753 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1753 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[58746] VGAM1753 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1753 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1753 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1753 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1753 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58747] The complementary binding of VGAM1753 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1753 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1753 host target RNA into VGAM1753 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58748] It is appreciated that VGAM1753 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1753 host target genes. The mRNA of each one of this plurality of VGAM1753 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1753 RNA, herein designated VGAM RNA, and which when bound by VGAM1753 RNA causes inhibition of translation of respective one or more VGAM1753 host target proteins.

[58749] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1753 gene, herein designated VGAM GENE, on one or more VGAM1753 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58750] It is yet further appreciated that a function of VGAM1753 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1753 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1753 correlate with, and may be deduced from, the identity of the host target genes which VGAM1753 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58751] Nucleotide sequences of the VGAM1753 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1753 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1753 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1753 are further described hereinbelow with reference to Table 1.

[58752] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1753 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1753 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[58753] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1753 gene, herein designated VGAM is inhibition of expression of VGAM1753 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1753 correlate with, and may be deduced from, the identity of the target genes which VGAM1753 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58754] EFG1 (Accession XM\_170611) is a VGAM1753 host target gene. EFG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFG1 BINDING SITE, designated SEQ ID:45397, to the nucleotide sequence of VGAM1753 RNA, herein designated VGAM RNA, also designated SEQ ID:4464.

[58755] A function of VGAM1753 is therefore inhibition of EFG1 (Accession XM\_170611), a gene which promotes the gtp-dependent translocation of the nascent protein chain from the a-site to the p-site of the ribosome in the mitochondria. Accordingly, utilities of VGAM1753 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with EFG1. The function of EFG1 has been established by previous studies. By EST database searching with rat Efg as probe, followed by PCR of a testis cDNA library, Gao et al. (2001) obtained cDNAs encoding mouse and human EFG1, which they called GFM. EFG1 encodes a deduced 751-amino acid protein that shares 84% and 89% sequence identity with rat Efg and mouse Gfm, respectively, and contains a conserved GTP-binding elongation factor signature and a GTP-binding domain composed of 3 motifs. Northern blot analysis revealed wide expression of 3.8- and 3.4-kb transcripts, abundant in heart, skeletal muscle, and testis, as well as testis-specific expression of a 2.9-kb transcript. Independently, Hammarsund et al. (2001) identified and characterized mitochondrial elongation factor-2 (EFG2; 606544) and used information contained in public databases to identify and clone the complete coding sequence of the human EFG1 gene on chromosome 3q25.

[58756] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58757] Gao, J.; Yu, L.; Zhang, P.; Jiang, J.; Chen, J.; Peng, J.; Wei,

Y.; Zhao, S. : Cloning and characterization of human and mouse mitochondrial elongation factor G, GFM and Gfm, and mapping of GFM to human chromosome

3q25.1–q26.2. Genomics 74: 109–114, 2001. ; and

[58758] Hammarsund, M.; Wilson, W.; Corcoran, M.; Merup, M.; Einhorn, S.; Grander, D.; Sangfelt, O. : Identification and characterization of two novel human mitochondrial elongation factor gene.

[58759] Further studies establishing the function and utilities of EFG1 are found in John Hopkins OMIM database record ID 606639, and in cited publications numbered 6124 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 6 (neurotransmitter transporter, dopamine), Member 3 (SLC6A3, Accession NM\_001044) is another VGAM1753 host target gene. SLC6A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A3 BINDING SITE, designated SEQ ID:6713, to the nucleotide sequence of VGAM1753 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4464.

[58760] Another function of VGAM1753 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, dopamine), Member 3 (SLC6A3, Accession NM\_001044), a gene which terminates the action of dopamine by its high affinity sodium-dependent reuptake into presynaptic terminals. Accordingly, utilities of VGAM1753 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A3. The function of SLC6A3 has been established by previous studies. Giros et al. (1996) found that the disruption of the mouse dopamine transporter gene results in spontaneous hyperlocomotion despite major adaptive changes such as decreases in neurotransmitter and receptor levels. In homozygous mice, dopamine persisted at least 100 times longer in the extracellular space, providing a biochemical explanation of the hyperdopaminergic phenotype and demonstrating the critical role of the transporter in regulating neurotransmission. The authors noted that the dopamine transporter is an obligatory target of cocaine and amphetamine, as demonstrated by the fact that these psychostimulants had no effect on locomotor activity or dopamine release and uptake in mice lacking the trans-

porter. Giros et al. (1996) stated that the DAT knockout mice should be an excellent tool for the study and development of drugs used in the management of dopaminergic dysfunction. There are similarities between the hyperdopaminergic phenotype of the knockout mice and some of the positive symptoms of schizophrenic patients. Specific blockade of the dopamine transporter with high-affinity inhibitors may be beneficial in illnesses such as Parkinson disease, where the effective levels of dopamine are markedly reduced.

[58761] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58762] Gainetdinov, R. R.; Wetsel, W. C.; Jones, S. R.; Levin, E. D.; Jaber, M.; Caron, M. G. : Role of serotonin in the paradoxical calming effect of psychostimulants on hyperactivity. Science 283: 397–401, 1999. ; and

[58763] Giros, B.; Jaber, M.; Jones, S. R.; Wightman, R. M.; Caron, M. G. : Hyperlocomotion and indifference to cocaine and amphetamine in mice lacking the dopamine receptor. Nature 370: 606–612, 1.

[58764] Further studies establishing the function and utilities of SLC6A3 are found in John Hopkins OMIM database record

ID 126455, and in cited publications numbered 2038–2046, 89 and 2293–2299 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. H2AV (Accession NM\_138635) is another VGAM1753 host target gene. H2AV BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H2AV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H2AV BINDING SITE, designated SEQ ID:28912, to the nucleotide sequence of VGAM1753 RNA, herein designated VGAM RNA, also designated SEQ ID:4464.

[58765] Another function of VGAM1753 is therefore inhibition of H2AV (Accession NM\_138635). Accordingly, utilities of VGAM1753 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H2AV. HMP19 (Accession XM\_113455) is another VGAM1753 host target gene. HMP19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMP19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity



of the nucleotide sequences of HMP19 BINDING SITE, designated SEQ ID:42273, to the nucleotide sequence of VGAM1753 RNA, herein designated VGAM RNA, also designated SEQ ID:4464.

[58766] Another function of VGAM1753 is therefore inhibition of HMP19 (Accession XM\_113455). Accordingly, utilities of VGAM1753 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMP19. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1754 (VGAM1754) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58767] VGAM1754 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1754 was detected is described hereinabove with reference to Figs. 1–8.

[58768] VGAM1754 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1754 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58769] VGAM1754 gene encodes a VGAM1754 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1754 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1754 precursor RNA is designated SEQ ID:1740, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1740 is located at position 9493 relative to the genome of Camelpox Virus.

[58770] VGAM1754 precursor RNA folds onto itself, forming VGAM1754 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58771] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1754 folded precursor RNA into VGAM1754 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1754 RNA is designated SEQ ID:4465, and is provided hereinbelow with reference to the sequence listing part.

[58772] VGAM1754 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1754 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1754 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58773] VGAM1754 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1754 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1754 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1754 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1754 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58774] The complementary binding of VGAM1754 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1754 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1754 host target RNA into VGAM1754 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58775] It is appreciated that VGAM1754 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1754 host target genes. The mRNA of each one of this plurality of VGAM1754 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1754 RNA, herein designated VGAM RNA, and which when bound by VGAM1754 RNA causes inhibition of translation of respective one or more VGAM1754 host target proteins.

[58776] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1754 gene, herein designated VGAM GENE, on one or more VGAM1754 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[58777] It is yet further appreciated that a function of VGAM1754 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1754 correlate with, and may be deduced from, the identity of the host target genes which VGAM1754 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58778] Nucleotide sequences of the VGAM1754 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1754 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1754 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1754 are further described hereinbelow with reference to Table 1.

[58779] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1754 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1754 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58780] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1754 gene, herein designated VGAM is inhibition of expression of VGAM1754 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1754 correlate with, and may be deduced from, the identity of the target genes which VGAM1754 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58781] Caveolin 1, Caveolae Protein, 22kDa (CAV1, Accession NM\_001753) is a VGAM1754 host target gene. CAV1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAV1 BINDING SITE, designated SEQ ID:7489, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58782] A function of VGAM1754 is therefore inhibition of Cave-

olin 1, Caveolae Protein, 22kDa (CAV1, Accession NM\_001753), a gene which may act as a scaffolding protein within caveolar membranes, and interacts directly with g-protein alpha subunits and can functionally regulate their activity. Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAV1. The function of CAV1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM331. Inducible T-cell Co-stimulator (ICOS, Accession NM\_012092) is another VGAM1754 host target gene. ICOS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICOS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICOS BINDING SITE, designated SEQ ID:14384, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58783] Another function of VGAM1754 is therefore inhibition of Inducible T-cell Co-stimulator (ICOS, Accession NM\_012092), a gene which forms homodimers and func-



tions as an inducible T-cell co-stimulator. Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICOS. The function of ICOS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18. Integrin, Alpha 11 (ITGA11, Accession NM\_012211) is another VGAM1754 host target gene. ITGA11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGA11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA11 BINDING SITE, designated SEQ ID:14513, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58784] Another function of VGAM1754 is therefore inhibition of Integrin, Alpha 11 (ITGA11, Accession NM\_012211), a gene which acts as a collagen I receptor. Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA11. The function of ITGA11 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. MADS Box Transcription Enhancer Factor 2, Polypeptide A (myocyte enhancer factor 2A) (MEF2A, Accession NM\_005587) is another VGAM1754 host target gene. MEF2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEF2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEF2A BINDING SITE, designated SEQ ID:12116, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58785] Another function of VGAM1754 is therefore inhibition of MADS Box Transcription Enhancer Factor 2, Polypeptide A (myocyte enhancer factor 2A) (MEF2A, Accession NM\_005587), a gene which binds a consensus sequence that regulates transcription. Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEF2A. The function of MEF2A and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM46. Midline 1 (Opitz/BBB syndrome) (MID1, Accession NM\_000381) is another VGAM1754 host target gene. MID1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MID1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MID1 BINDING SITE, designated SEQ ID:5955, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58786] Another function of VGAM1754 is therefore inhibition of Midline 1 (Opitz/BBB syndrome) (MID1, Accession NM\_000381). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MID1. Mucin 3B (MUC3B, Accession XM\_168578) is another VGAM1754 host target gene. MUC3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MUC3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC3B BINDING SITE, designated SEQ

ID:45257, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58787] Another function of VGAM1754 is therefore inhibition of Mucin 3B (MUC3B, Accession XM\_168578), a gene which provides a protective, lubricating barrier against particles and infectious agents at mucosal surfaces. Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC3B. The function of MUC3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Sialidase 3 (membrane sialidase) (NEU3, Accession NM\_006656) is another VGAM1754 host target gene. NEU3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEU3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEU3 BINDING SITE, designated SEQ ID:13457, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58788] Another function of VGAM1754 is therefore inhibition of Sialidase 3 (membrane sialidase) (NEU3, Accession NM\_006656). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEU3. Plastin 3 (T isoform) (PLS3, Accession NM\_005032) is another VGAM1754 host target gene. PLS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLS3 BINDING SITE, designated SEQ ID:11473, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58789] Another function of VGAM1754 is therefore inhibition of Plastin 3 (T isoform)(PLS3, Accession NM\_005032), a gene which binds actin. Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLS3. The function of PLS3 has been established by previous studies. Plastins are a family of actin-binding proteins that are differentially expressed in normal and malignant cells. Lin et al.

(1988) isolated partial cDNAs encoding T-plastin and L-plastin (OMIM Ref. No. 153430) from a transformed human fibroblast cDNA library. The C-terminal 570 amino acids of the T-plastin and L-plastin proteins are 83% identical. By 2-dimensional gel electrophoresis of human cell extracts, Lin et al. (1988) showed that T-plastin is expressed as 2 equally abundant isoforms. Northern blot analysis revealed that T-plastin is expressed as a 3.4-kb mRNA in normal cells of solid tissues and in transformed fibroblasts. Using anchored PCR, Lin et al. (1990) identified the 5-prime end of the T-plastin mRNA. The T-plastin transcript has 2 possible translation initiation codons which would result in predicted 627- and 630-amino acid proteins. The authors constructed 2 modified T-plastin cDNAs containing either the first or the second initiation codon. Expression of these cDNAs in *E. coli* resulted in the synthesis of 2 distinct T-plastins with the same isoelectric points and apparent molecular weights as the 2 T-plastins present in human cells. Lin et al. (1990) found that T-plastin contains a potential calcium-binding site near the N terminus. Lin et al. (1993) reported that both the L-plastin and T-plastin genes contain 16 exons and span approximately 90 kb

[58790] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58791] Lin, C.-S.; Aebersold, R. H.; Leavitt, J. : Correction of the N-terminal sequences of the human plastin isoforms by using anchored polymerase chain reaction: identification of a potential calcium-binding domain. *Molec. Cell. Biol.* 10: 1818-1821, 1990. ; and

[58792] Lin, C.-S.; Park, T.; Chen, Z. P.; Leavitt, J. : Human plastin genes: comparative gene structure, chromosome location, and differential expression in normal and neoplastic cells. *J. Biol.*

[58793] Further studies establishing the function and utilities of PLS3 are found in John Hopkins OMIM database record ID 300131, and in cited publications numbered 65 and 10989 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SPS2 (Accession NM\_012248) is another VGAM1754 host target gene. SPS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of SPS2 BINDING SITE, designated SEQ ID:14555, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58794] Another function of VGAM1754 is therefore inhibition of SPS2 (Accession NM\_012248), a gene which synthesizes selenophosphate from selenide and ATP. Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPS2. The function of SPS2 has been established by previous studies. By screening activated CD8 (see OMIM Ref. No. 186910)–positive T cells with mouse Sps2, a homolog of *E. coli* selD, as the probe, Guimaraes et al. (1996) isolated a cDNA encoding human SPS2. The deduced 448–amino acid SPS2 protein contains Walker A– and B–like motifs, which are characteristic of alpha/beta nucleotide–binding folds. The SPS2 Walker A–like motif is a gly–rich site that includes the sec residue. Northern blot analysis revealed preferential expression of a 2.3–kb transcript in mouse tissues that produce selenoproteins, with lower expression in sites of blood cell development. Levels of Sps2 mRNA were upregulated upon activation of CD4 (OMIM Ref. No. 186940)–positive lymphocytes. Western blot analysis showed that Sps2 levels were 20–fold



higher when the 3-prime untranslated region (UTR) of Sps2 was included in the expression construct in transfected cells. Southern blot analysis indicated that SPS2 is well-conserved in mammals

[58795] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58796] Guimaraes, M. J.; Peterson, D.; Vicari, A.; Cocks, B. G.; Copeland, N. G.; Gilbert, D. J.; Jenkins, N. A.; Ferrick, D. A.; Kastelein, R. A.; Bazan, J. F.; Zlotnik, A. : Identification of a novel selD homolog from eukaryotes, bacteria, and archaea: is there an autoregulatory mechanism in selenocysteine metabolism? Proc. Nat. Acad. Sci. 93: 15086-15091, 1996. ; and

[58797] Lescure, A.; Gautheret, D.; Carbon, P.; Krol, A. : Novel selenoproteins identified in silico and in vivo by using a conserved RNA structural motif. J. Biol. Chem. 274: 38147-38154, 1999.

[58798] Further studies establishing the function and utilities of SPS2 are found in John Hopkins OMIM database record ID 606218, and in cited publications numbered 6590 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TRAP240 (Accession

NM\_005121) is another VGAM1754 host target gene. TRAP240 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAP240, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAP240 BINDING SITE, designated SEQ ID:11604, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58799] Another function of VGAM1754 is therefore inhibition of TRAP240 (Accession NM\_005121), a gene which Subunit of TRAP thyroid hormone receptor-associated protein complex; coactivator for nuclear receptors. Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAP240. The function of TRAP240 has been established by previous studies. For background information on thyroid hormone receptor-associated proteins (TRAPs), see 300182. Using a HeLa cell line, Ito et al. (1999) cloned TRAP240, the gene encoding the 240-kD subunit of the TRAP complex. The TRAP240 cDNA encodes a 2,174-amino acid protein that shows a regional identity of

29% and a similarity of 46% with a hypothetical *C. elegans* protein (CEK08F8 and CEF07H5). It shows no obvious relationship with known consensus sequences, other than 2 ligand-dependent nuclear hormone receptor signature recognition motifs (LXXLL sequences) at positions 1188–1192 and 1279–1283, and a short leucine zipper at position 1331–1352. Northern blot analysis of multiple human tissues showed that the TRAP240 gene is ubiquitously expressed as an approximately 11.5-kb transcript. Nagase et al. (1998) also cloned the cDNA encoding TRAP240, which they referred to as KIAA0593, from a human brain cDNA library. By analysis of a human-rodent hybrid panel, Nagase et al. (1998) mapped the TRAP240 gene to chromosome 17

[58800] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58801] Ito, M.; Yuan, C.-X.; Malik, S.; Gu, W.; Fondell, J. D.; Yamamura, S.; Fu, Z.-Y.; Zhang, X.; Qin, J.; Roeder, R. G. : Identity between TRAP and SMCC complexes indicates novel pathways for the function of nuclear receptors and diverse mammalian activators. *Molec. Cell* 3: 361–370, 1999. ; and

[58802] Nagase, T.; Ishikawa, K.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. IX. The complete sequences of 100.

[58803] Further studies establishing the function and utilities of TRAP240 are found in John Hopkins OMIM database record ID 603808, and in cited publications numbered 11384 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248) is another VGAM1754 host target gene. AKAP11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP11 BINDING SITE, designated SEQ ID:18365, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58804] Another function of VGAM1754 is therefore inhibition of A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248). Accordingly, utilities of VGAM1754 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP11. CAP (Accession NM\_006367) is another VGAM1754 host target gene. CAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAP BINDING SITE, designated SEQ ID:13056, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58805] Another function of VGAM1754 is therefore inhibition of CAP (Accession NM\_006367). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAP. CGI-01 (Accession NM\_015935) is another VGAM1754 host target gene. CGI-01 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CGI-01, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGI-01 BINDING SITE, designated SEQ ID:18054, to the nucleotide sequence of

VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58806] Another function of VGAM1754 is therefore inhibition of CGI-01 (Accession NM\_015935). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGI-01. DKFZP434D1335 (Accession XM\_036578) is another VGAM1754 host target gene. DKFZP434D1335 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434D1335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434D1335 BINDING SITE, designated SEQ ID:32467, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58807] Another function of VGAM1754 is therefore inhibition of DKFZP434D1335 (Accession XM\_036578). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434D1335. FLJ10498 (Accession NM\_018115) is another VGAM1754 host target gene. FLJ10498 BIND-

ING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10498, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10498 BINDING SITE, designated SEQ ID:19887, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58808] Another function of VGAM1754 is therefore inhibition of FLJ10498 (Accession NM\_018115). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10498. FLJ10901 (Accession NM\_018265) is another VGAM1754 host target gene. FLJ10901 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10901, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10901 BINDING SITE, designated SEQ ID:20231, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58809] Another function of VGAM1754 is therefore inhibition of

FLJ10901 (Accession NM\_018265). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10901. FLJ14547 (Accession NM\_032804) is another VGAM1754 host target gene. FLJ14547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14547 BINDING SITE, designated SEQ ID:26561, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58810] Another function of VGAM1754 is therefore inhibition of FLJ14547 (Accession NM\_032804). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14547. FLJ22693 (Accession NM\_022750) is another VGAM1754 host target gene. FLJ22693 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-



plementarity of the nucleotide sequences of FLJ22693 BINDING SITE, designated SEQ ID:22973, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58811] Another function of VGAM1754 is therefore inhibition of FLJ22693 (Accession NM\_022750). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22693. HBP1 (Accession NM\_012257) is another VGAM1754 host target gene. HBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HBP1 BINDING SITE, designated SEQ ID:14562, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58812] Another function of VGAM1754 is therefore inhibition of HBP1 (Accession NM\_012257). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HBP1. HCA3 (Accession NM\_138703) is another VGAM1754 host

target gene. HCA3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HCA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA3 BINDING SITE, designated SEQ ID:28952, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58813] Another function of VGAM1754 is therefore inhibition of HCA3 (Accession NM\_138703). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCA3. HCNGP (Accession NM\_013260) is another VGAM1754 host target gene. HCNGP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HCNGP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCNGP BINDING SITE, designated SEQ ID:14930, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58814] Another function of VGAM1754 is therefore inhibition of HCNGP (Accession NM\_013260). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCNGP. MGC15429 (Accession NM\_032750) is another VGAM1754 host target gene. MGC15429 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15429 BINDING SITE, designated SEQ ID:26485, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58815] Another function of VGAM1754 is therefore inhibition of MGC15429 (Accession NM\_032750). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15429. Nudix (nucleoside diphosphate linked moiety X)-type Motif 11 (NUDT11, Accession XM\_010230) is another VGAM1754 host target gene. NUDT11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDT11, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUDT11 BINDING SITE, designated SEQ ID:30138, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58816] Another function of VGAM1754 is therefore inhibition of Nudix (nucleoside diphosphate linked moiety X)-type Motif 11 (NUDT11, Accession XM\_010230). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUDT11. P5-1 (Accession NM\_006674) is another VGAM1754 host target gene. P5-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P5-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P5-1 BINDING SITE, designated SEQ ID:13493, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58817] Another function of VGAM1754 is therefore inhibition of P5-1 (Accession NM\_006674). Accordingly, utilities of

VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P5-1. Parvin, Alpha (PARVA, Accession NM\_018222) is another VGAM1754 host target gene. PARVA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PARVA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PARVA BINDING SITE, designated SEQ ID:20144, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58818] Another function of VGAM1754 is therefore inhibition of Parvin, Alpha (PARVA, Accession NM\_018222). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PARVA. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM\_028840) is another VGAM1754 host target gene. PPP1R16B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R16B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of PPP1R16B BINDING SITE, designated SEQ ID:30768, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58819] Another function of VGAM1754 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM\_028840). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R16B. PRO0245 (Accession NM\_014122) is another VGAM1754 host target gene. PRO0245 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0245, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0245 BINDING SITE, designated SEQ ID:15377, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58820] Another function of VGAM1754 is therefore inhibition of PRO0245 (Accession NM\_014122). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PRO0245. LOC139174 (Accession XM\_066525) is another VGAM1754 host target gene. LOC139174 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC139174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139174 BINDING SITE, designated SEQ ID:37328, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58821] Another function of VGAM1754 is therefore inhibition of LOC139174 (Accession XM\_066525). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139174. LOC148738 (Accession NM\_145277) is another VGAM1754 host target gene. LOC148738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148738 BINDING SITE, designated SEQ ID:29789, to the nucleotide sequence of VGAM1754 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4465.

[58822] Another function of VGAM1754 is therefore inhibition of LOC148738 (Accession NM\_145277). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148738. LOC152059 (Accession XM\_087372) is another VGAM1754 host target gene. LOC152059 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152059, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152059 BINDING SITE, designated SEQ ID:39205, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58823] Another function of VGAM1754 is therefore inhibition of LOC152059 (Accession XM\_087372). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152059. LOC154881 (Accession XM\_088063) is another VGAM1754 host target gene. LOC154881 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154881, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154881 BINDING SITE, designated SEQ ID:39500, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58824] Another function of VGAM1754 is therefore inhibition of LOC154881 (Accession XM\_088063). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154881. LOC196759 (Accession XM\_113601) is another VGAM1754 host target gene. LOC196759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196759 BINDING SITE, designated SEQ ID:42291, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58825] Another function of VGAM1754 is therefore inhibition of LOC196759 (Accession XM\_113601). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC196759. LOC220486 (Accession XM\_165391) is another VGAM1754 host target gene. LOC220486 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC220486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220486 BINDING SITE, designated SEQ ID:43616, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58826] Another function of VGAM1754 is therefore inhibition of LOC220486 (Accession XM\_165391). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220486. LOC257273 (Accession XM\_170970) is another VGAM1754 host target gene. LOC257273 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257273 BINDING SITE, designated SEQ ID:45745, to

the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58827] Another function of VGAM1754 is therefore inhibition of LOC257273 (Accession XM\_170970). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257273. LOC92573 (Accession XM\_045884) is another VGAM1754 host target gene. LOC92573 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92573 BINDING SITE, designated SEQ ID:34592, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58828] Another function of VGAM1754 is therefore inhibition of LOC92573 (Accession XM\_045884). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92573. LOC96597 (Accession XM\_039922) is another VGAM1754 host target gene. LOC96597 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC96597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC96597 BINDING SITE, designated SEQ ID:33227, to the nucleotide sequence of VGAM1754 RNA, herein designated VGAM RNA, also designated SEQ ID:4465.

[58829] Another function of VGAM1754 is therefore inhibition of LOC96597 (Accession XM\_039922). Accordingly, utilities of VGAM1754 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC96597. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1755 (VGAM1755) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58830] VGAM1755 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1755 was detected is described hereinabove with reference to Figs. 1-8.

[58831] VGAM1755 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Camelpox Virus.

VGAM1755 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58832] VGAM1755 gene encodes a VGAM1755 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1755 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1755 precursor RNA is designated SEQ ID:1741, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1741 is located at position 5746 relative to the genome of Camelpox Virus.

[58833] VGAM1755 precursor RNA folds onto itself, forming VGAM1755 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58834] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1755 folded precursor RNA into VGAM1755 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1755 RNA is designated SEQ ID:4466, and is provided hereinbelow with reference to the sequence listing part.

[58835] VGAM1755 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1755 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1755 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58836] VGAM1755 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1755 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1755 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1755 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1755 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58837] The complementary binding of VGAM1755 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1755 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1755

host target RNA into VGAM1755 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58838] It is appreciated that VGAM1755 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1755 host target genes. The mRNA of each one of this plurality of VGAM1755 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1755 RNA, herein designated VGAM RNA, and which when bound by VGAM1755 RNA causes inhibition of translation of respective one or more VGAM1755 host target proteins.

[58839] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1755 gene, herein designated VGAM GENE, on one or more VGAM1755 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58840] It is yet further appreciated that a function of VGAM1755 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1755 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1755 correlate with, and may be deduced from, the identity of the host target genes which VGAM1755 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58841] Nucleotide sequences of the VGAM1755 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1755 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1755 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1755 are further

described hereinbelow with reference to Table 1.

[58842] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1755 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1755 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58843] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1755 gene, herein designated VGAM is inhibition of expression of VGAM1755 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1755 correlate with, and may be deduced from, the identity of the target genes which VGAM1755 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58844] Monoamine Oxidase B (MAOB, Accession XM\_010261) is a VGAM1755 host target gene. MAOB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAOB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAOB BINDING SITE,

designated SEQ ID:30147, to the nucleotide sequence of VGAM1755 RNA, herein designated VGAM RNA, also designated SEQ ID:4466.

[58845] A function of VGAM1755 is therefore inhibition of Monoamine Oxidase B (MAOB, Accession XM\_010261). Accordingly, utilities of VGAM1755 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAOB. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1756 (VGAM1756) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58846] VGAM1756 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1756 was detected is described hereinabove with reference to Figs. 1–8.

[58847] VGAM1756 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1756 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58848] VGAM1756 gene encodes a VGAM1756 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1756 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1756 precursor RNA is designated SEQ ID:1742, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1742 is located at position 7373 relative to the genome of Camelpox Virus.

[58849] VGAM1756 precursor RNA folds onto itself, forming VGAM1756 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58850] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1756 folded precursor RNA into VGAM1756 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1756 RNA is designated SEQ ID:4467, and is provided hereinbelow with reference to the sequence listing part.

[58851] VGAM1756 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1756 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1756 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58852] VGAM1756 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1756 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1756 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1756 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1756 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58853] The complementary binding of VGAM1756 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1756 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1756 host target RNA into VGAM1756 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58854] It is appreciated that VGAM1756 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1756 host target genes. The mRNA of each one of this plurality of VGAM1756 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1756 RNA, herein designated VGAM RNA, and which when bound by VGAM1756 RNA causes inhibition of translation of respective one or more VGAM1756 host target proteins.

[58855] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1756 gene, herein designated VGAM GENE, on one or more VGAM1756 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[58856] It is yet further appreciated that a function of VGAM1756 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1756 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1756 correlate with, and may be deduced from, the identity of the host target genes which VGAM1756 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58857] Nucleotide sequences of the VGAM1756 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1756 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1756 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1756 are further described hereinbelow with reference to Table 1.

[58858] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1756 host target RNA, and



schematic representation of the complementarity of each of these host target binding sites to VGAM1756 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58859] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1756 gene, herein designated VGAM is inhibition of expression of VGAM1756 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1756 correlate with, and may be deduced from, the identity of the target genes which VGAM1756 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58860] NESG1 (Accession NM\_012337) is a VGAM1756 host target gene. NESG1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NESG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NESG1 BINDING SITE, designated SEQ ID:14733, to the nucleotide sequence of VGAM1756 RNA, herein designated VGAM RNA, also designated SEQ ID:4467.

[58861] A function of VGAM1756 is therefore inhibition of NESG1

(Accession NM\_012337). Accordingly, utilities of VGAM1756 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NESG1. LOC148638 (Accession XM\_086259) is another VGAM1756 host target gene. LOC148638 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148638, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148638 BINDING SITE, designated SEQ ID:38569, to the nucleotide sequence of VGAM1756 RNA, herein designated VGAM RNA, also designated SEQ ID:4467.

[58862] Another function of VGAM1756 is therefore inhibition of LOC148638 (Accession XM\_086259). Accordingly, utilities of VGAM1756 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148638. LOC152359 (Accession XM\_098213) is another VGAM1756 host target gene. LOC152359 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152359, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC152359 BINDING SITE, designated SEQ ID:41492, to the nucleotide sequence of VGAM1756 RNA, herein designated VGAM RNA, also designated SEQ ID:4467.

[58863] Another function of VGAM1756 is therefore inhibition of LOC152359 (Accession XM\_098213). Accordingly, utilities of VGAM1756 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152359. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1757 (VGAM1757) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58864] VGAM1757 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1757 was detected is described hereinabove with reference to Figs. 1–8.

[58865] VGAM1757 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1757 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[58866] VGAM1757 gene encodes a VGAM1757 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1757 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1757 precursor RNA is designated SEQ ID:1743, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1743 is located at position 5203 relative to the genome of Camelpox Virus.

[58867] VGAM1757 precursor RNA folds onto itself, forming VGAM1757 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58868] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1757 folded precursor RNA into VGAM1757 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1757 RNA is designated SEQ ID:4468, and is provided hereinbelow with reference to the sequence listing part.

[58869] VGAM1757 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1757 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1757 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58870] VGAM1757 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1757 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1757 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1757 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1757 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58871] The complementary binding of VGAM1757 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1757 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1757 host target RNA into VGAM1757 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58872] It is appreciated that VGAM1757 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1757 host target genes. The mRNA of each one of this plurality of VGAM1757 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1757 RNA, herein designated VGAM RNA, and which when bound by VGAM1757 RNA causes inhibition of translation of respective one or more VGAM1757 host target proteins.

[58873] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1757 gene, herein designated VGAM GENE, on one or more VGAM1757 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58874] It is yet further appreciated that a function of VGAM1757 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1757 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1757 correlate with, and may be deduced from, the identity of the host target genes which VGAM1757 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58875] Nucleotide sequences of the VGAM1757 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1757 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1757 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1757 are further described hereinbelow with reference to Table 1.

[58876] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of



Fig. 1, found on VGAM1757 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1757 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58877] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1757 gene, herein designated VGAM is inhibition of expression of VGAM1757 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1757 correlate with, and may be deduced from, the identity of the target genes which VGAM1757 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58878] Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog 2 (mouse) (MEIS2, Accession NM\_020149) is a VGAM1757 host target gene. MEIS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEIS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEIS2 BINDING SITE, designated SEQ ID:21344, to the nucleotide sequence of VGAM1757 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4468.

[58879] A function of VGAM1757 is therefore inhibition of Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog 2 (mouse) (MEIS2, Accession NM\_020149), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1757 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEIS2. The function of MEIS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1244.BS69 (Accession NM\_006624) is another VGAM1757 host target gene. BS69 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BS69, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BS69 BINDING SITE, designated SEQ ID:13405, to the nucleotide sequence of VGAM1757 RNA, herein designated VGAM RNA, also designated SEQ ID:4468.

[58880] Another function of VGAM1757 is therefore inhibition of BS69 (Accession NM\_006624). Accordingly, utilities of VGAM1757 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with BS69. Chromosome X Open Reading Frame 1 (CXorf1, Accession NM\_004709) is another VGAM1757 host target gene. CXorf1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CXorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXorf1 BINDING SITE, designated SEQ ID:11053, to the nucleotide sequence of VGAM1757 RNA, herein designated VGAM RNA, also designated SEQ ID:4468.

[58881] Another function of VGAM1757 is therefore inhibition of Chromosome X Open Reading Frame 1 (CXorf1, Accession NM\_004709). Accordingly, utilities of VGAM1757 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXorf1. FLJ21791 (Accession XM\_028958) is another VGAM1757 host target gene. FLJ21791 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21791, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of FLJ21791 BINDING SITE, designated SEQ ID:30807, to the nucleotide sequence of VGAM1757 RNA, herein designated VGAM RNA, also designated SEQ ID:4468.

[58882] Another function of VGAM1757 is therefore inhibition of FLJ21791 (Accession XM\_028958). Accordingly, utilities of VGAM1757 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21791. LANO (Accession NM\_025168) is another VGAM1757 host target gene. LANO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LANO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LANO BINDING SITE, designated SEQ ID:24804, to the nucleotide sequence of VGAM1757 RNA, herein designated VGAM RNA, also designated SEQ ID:4468.

[58883] Another function of VGAM1757 is therefore inhibition of LANO (Accession NM\_025168). Accordingly, utilities of VGAM1757 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LANO. Proteasome (prosome, macropain) Inhibitor Subunit 1

(PI31) (PSMF1, Accession NM\_006814) is another VGAM1757 host target gene. PSMF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PSMF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMF1 BINDING SITE, designated SEQ ID:13686, to the nucleotide sequence of VGAM1757 RNA, herein designated VGAM RNA, also designated SEQ ID:4468.

[58884] Another function of VGAM1757 is therefore inhibition of Proteasome (prosome, macropain) Inhibitor Subunit 1 (PI31) (PSMF1, Accession NM\_006814). Accordingly, utilities of VGAM1757 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMF1. LOC115129 (Accession XM\_055292) is another VGAM1757 host target gene. LOC115129 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC115129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115129 BINDING SITE, designated SEQ ID:36249, to

the nucleotide sequence of VGAM1757 RNA, herein designated VGAM RNA, also designated SEQ ID:4468.

[58885] Another function of VGAM1757 is therefore inhibition of LOC115129 (Accession XM\_055292). Accordingly, utilities of VGAM1757 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115129. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1758 (VGAM1758) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58886] VGAM1758 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1758 was detected is described hereinabove with reference to Figs. 1–8.

[58887] VGAM1758 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus.

VGAM1758 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58888] VGAM1758 gene encodes a VGAM1758 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1758 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1758 precursor RNA is designated SEQ ID:1744, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1744 is located at position 60 relative to the genome of Camelpox Virus.

[58889] VGAM1758 precursor RNA folds onto itself, forming VGAM1758 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58890] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1758 folded precursor RNA into VGAM1758 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1758 RNA is designated SEQ ID:4469, and is provided hereinbelow with reference to the sequence listing part.

[58891] VGAM1758 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1758 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1758 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58892] VGAM1758 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1758 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1758 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding



sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1758 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1758 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58893] The complementary binding of VGAM1758 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1758 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1758 host target RNA into VGAM1758 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58894] It is appreciated that VGAM1758 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1758 host target genes. The mRNA of each one of this plurality of VGAM1758 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1758 RNA, herein designated VGAM RNA, and which when bound by VGAM1758 RNA causes inhibition of translation of respective one or more VGAM1758 host target proteins.

[58895] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1758 gene, herein designated VGAM GENE, on one or more VGAM1758 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[58896] It is yet further appreciated that a function of VGAM1758 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1758 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1758 correlate with, and may be deduced from, the identity of the host target genes which VGAM1758 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58897] Nucleotide sequences of the VGAM1758 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1758 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1758 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1758 are further described hereinbelow with reference to Table 1.

[58898] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1758 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1758 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58899] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1758 gene, herein designated VGAM is inhibition of expression of VGAM1758 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1758 correlate with, and may be deduced from, the identity of the target genes which VGAM1758 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58900] LOC152078 (Accession XM\_087376) is a VGAM1758 host target gene. LOC152078 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152078 BINDING SITE, designated SEQ ID:39213, to the nucleotide sequence of VGAM1758 RNA, herein designated VGAM RNA, also designated SEQ ID:4469.

[58901] A function of VGAM1758 is therefore inhibition of LOC152078 (Accession XM\_087376). Accordingly, utilities

of VGAM1758 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152078. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1759 (VGAM1759) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58902] VGAM1759 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1759 was detected is described hereinabove with reference to Figs. 1–8.

[58903] VGAM1759 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV–2). VGAM1759 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58904] VGAM1759 gene encodes a VGAM1759 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1759 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu–

cleotide sequence of VGAM1759 precursor RNA is designated SEQ ID:1745, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1745 is located at position 12109 relative to the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2).

- [58905] VGAM1759 precursor RNA folds onto itself, forming VGAM1759 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [58906] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1759 folded precursor RNA into VGAM1759 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide se-

quence of VGAM1759 RNA is designated SEQ ID:4470, and is provided hereinbelow with reference to the sequence listing part.

[58907] VGAM1759 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1759 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1759 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58908] VGAM1759 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1759 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1759 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1759 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1759 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[58909] The complementary binding of VGAM1759 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1759 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1759 host target RNA into VGAM1759 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58910] It is appreciated that VGAM1759 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1759 host target genes. The mRNA of each one of this plurality of VGAM1759 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1759 RNA, herein designated VGAM RNA, and which when bound by VGAM1759 RNA causes inhibition of translation of respective one or more VGAM1759 host target proteins.

[58911] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1759 gene, herein designated VGAM GENE, on one or more VGAM1759 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58912] It is yet further appreciated that a function of VGAM1759

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1759 include diagnosis, prevention and treatment of viral infection by Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). Specific functions, and accordingly utilities, of VGAM1759 correlate with, and may be deduced from, the identity of the host target genes which VGAM1759 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58913] Nucleotide sequences of the VGAM1759 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1759 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1759 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1759 are further described hereinbelow with reference to Table 1.

[58914] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1759 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1759 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58915] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1759 gene, herein designated VGAM is inhibition of expression of VGAM1759 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1759 correlate with, and may be deduced from, the identity of the target genes which VGAM1759 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58916] ADG-90 (Accession NM\_033069) is a VGAM1759 host target gene. ADG-90 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADG-90, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADG-90 BINDING SITE, designated SEQ ID:26934, to the nucleotide sequence of VGAM1759 RNA, herein designated VGAM RNA, also designated SEQ ID:4470.

[58917] A function of VGAM1759 is therefore inhibition of ADG-90 (Accession NM\_033069). Accordingly, utilities of VGAM1759 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADG-90. NEU4 (Accession NM\_080741) is another VGAM1759

host target gene. NEU4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NEU4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEU4 BINDING SITE, designated SEQ ID:28026, to the nucleotide sequence of VGAM1759 RNA, herein designated VGAM RNA, also designated SEQ ID:4470.

[58918] Another function of VGAM1759 is therefore inhibition of NEU4 (Accession NM\_080741). Accordingly, utilities of VGAM1759 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEU4. LOC149535 (Accession XM\_086567) is another VGAM1759 host target gene. LOC149535 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149535 BINDING SITE, designated SEQ ID:38771, to the nucleotide sequence of VGAM1759 RNA, herein designated VGAM RNA, also designated SEQ ID:4470.

[58919] Another function of VGAM1759 is therefore inhibition of LOC149535 (Accession XM\_086567). Accordingly, utilities of VGAM1759 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149535. LOC200301 (Accession XM\_114197) is another VGAM1759 host target gene. LOC200301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200301 BINDING SITE, designated SEQ ID:42779, to the nucleotide sequence of VGAM1759 RNA, herein designated VGAM RNA, also designated SEQ ID:4470.

[58920] Another function of VGAM1759 is therefore inhibition of LOC200301 (Accession XM\_114197). Accordingly, utilities of VGAM1759 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200301. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1760 (VGAM1760) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[58921] VGAM1760 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1760 was detected is described hereinabove with reference to Figs. 1–8.

[58922] VGAM1760 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV–2). VGAM1760 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58923] VGAM1760 gene encodes a VGAM1760 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1760 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1760 precursor RNA is designated SEQ ID:1746, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1746 is located at position 7567 relative to the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV–2).

[58924] VGAM1760 precursor RNA folds onto itself, forming

VGAM1760 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58925] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1760 folded precursor RNA into VGAM1760 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1760 RNA is designated SEQ ID:4471, and is provided hereinbelow with reference to the sequence listing part.

[58926] VGAM1760 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1760 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1760 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58927] VGAM1760 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1760 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1760 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1760 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1760 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example



only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[58928] The complementary binding of VGAM1760 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1760 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1760 host target RNA into VGAM1760 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58929] It is appreciated that VGAM1760 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1760 host target genes. The mRNA of each one of this plurality of VGAM1760 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1760 RNA, herein designated VGAM RNA, and which when bound by VGAM1760 RNA causes inhibition of translation of respective one or more VGAM1760 host target proteins.

[58930] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1760 gene, herein designated VGAM GENE, on one or more VGAM1760 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58931] It is yet further appreciated that a function of VGAM1760 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1760 include diagnosis, prevention and treatment of viral infection by Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). Specific functions, and accordingly utilities, of VGAM1760 correlate with, and may be deduced from, the identity of the host target genes which

VGAM1760 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58932] Nucleotide sequences of the VGAM1760 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1760 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1760 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1760 are further described hereinbelow with reference to Table 1.

[58933] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1760 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1760 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58934] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1760 gene, herein designated VGAM is inhibition of expression of VGAM1760 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1760 correlate with, and may be deduced from, the identity of the target genes which VGAM1760 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[58935] Cartilage Acidic Protein 1 (CRTAC1, Accession NM\_018058) is a VGAM1760 host target gene. CRTAC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CRTAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRTAC1 BINDING SITE, designated SEQ ID:19826, to the nucleotide sequence of VGAM1760 RNA, herein designated VGAM RNA, also designated SEQ ID:4471.

[58936] A function of VGAM1760 is therefore inhibition of Cartilage Acidic Protein 1 (CRTAC1, Accession NM\_018058). Accordingly, utilities of VGAM1760 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRTAC1. DKFZP434J193 (Accession XM\_048452) is another VGAM1760 host target gene. DKFZP434J193 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434J193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of DKFZP434J193 BINDING SITE, designated SEQ ID:35160, to the nucleotide sequence of VGAM1760 RNA, herein designated VGAM RNA, also designated SEQ ID:4471.

[58937] Another function of VGAM1760 is therefore inhibition of DKFZP434J193 (Accession XM\_048452). Accordingly, utilities of VGAM1760 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434J193. Methylene Tetrahydrofolate Dehydrogenase (NAD<sup>+</sup> dependent), Methenyltetrahydrofolate Cyclohydrolase (MTHFD2, Accession NM\_006636) is another VGAM1760 host target gene. MTHFD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTHFD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTHFD2 BINDING SITE, designated SEQ ID:13430, to the nucleotide sequence of VGAM1760 RNA, herein designated VGAM RNA, also designated SEQ ID:4471.

[58938] Another function of VGAM1760 is therefore inhibition of Methylene Tetrahydrofolate Dehydrogenase (NAD<sup>+</sup> dependent), Methenyltetrahydrofolate Cyclohydrolase

(MTHFD2, Accession NM\_006636). Accordingly, utilities of VGAM1760 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTHFD2. SMC1 Structural Maintenance of Chromosomes 1-like 1 (yeast) (SMC1L1, Accession XM\_050403) is another VGAM1760 host target gene. SMC1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMC1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMC1L1 BINDING SITE, designated SEQ ID:35616, to the nucleotide sequence of VGAM1760 RNA, herein designated VGAM RNA, also designated SEQ ID:4471.

[58939] Another function of VGAM1760 is therefore inhibition of SMC1 Structural Maintenance of Chromosomes 1-like 1 (yeast) (SMC1L1, Accession XM\_050403). Accordingly, utilities of VGAM1760 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMC1L1. LOC145483 (Accession XM\_085156) is another VGAM1760 host target gene. LOC145483 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145483, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145483 BINDING SITE, designated SEQ ID:37881, to the nucleotide sequence of VGAM1760 RNA, herein designated VGAM RNA, also designated SEQ ID:4471.

[58940] Another function of VGAM1760 is therefore inhibition of LOC145483 (Accession XM\_085156). Accordingly, utilities of VGAM1760 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145483. LOC158476 (Accession XM\_098955) is another VGAM1760 host target gene. LOC158476 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158476 BINDING SITE, designated SEQ ID:41996, to the nucleotide sequence of VGAM1760 RNA, herein designated VGAM RNA, also designated SEQ ID:4471.

[58941] Another function of VGAM1760 is therefore inhibition of LOC158476 (Accession XM\_098955). Accordingly, utilities of VGAM1760 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC158476. LOC161823 (Accession XM\_091156) is another VGAM1760 host target gene. LOC161823 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC161823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161823 BINDING SITE, designated SEQ ID:40032, to the nucleotide sequence of VGAM1760 RNA, herein designated VGAM RNA, also designated SEQ ID:4471.

[58942] Another function of VGAM1760 is therefore inhibition of LOC161823 (Accession XM\_091156). Accordingly, utilities of VGAM1760 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161823. LOC164295 (Accession XM\_092767) is another VGAM1760 host target gene. LOC164295 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164295 BINDING SITE, designated SEQ ID:40140, to



the nucleotide sequence of VGAM1760 RNA, herein designated VGAM RNA, also designated SEQ ID:4471.

[58943] Another function of VGAM1760 is therefore inhibition of LOC164295 (Accession XM\_092767). Accordingly, utilities of VGAM1760 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164295. LOC92661 (Accession XM\_046465) is another VGAM1760 host target gene. LOC92661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92661 BINDING SITE, designated SEQ ID:34725, to the nucleotide sequence of VGAM1760 RNA, herein designated VGAM RNA, also designated SEQ ID:4471.

[58944] Another function of VGAM1760 is therefore inhibition of LOC92661 (Accession XM\_046465). Accordingly, utilities of VGAM1760 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92661. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1761 (VGAM1761) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58945] VGAM1761 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1761 was detected is described hereinabove with reference to Figs. 1–8.

[58946] VGAM1761 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV–2). VGAM1761 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58947] VGAM1761 gene encodes a VGAM1761 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1761 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1761 precursor RNA is designated SEQ ID:1747, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1747 is located at position 11998 relative to the genome of Bovine Viral Diarrhea Virus Genotype 2

(BVDV-2).

[58948] VGAM1761 precursor RNA folds onto itself, forming VGAM1761 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[58949] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1761 folded precursor RNA into VGAM1761 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1761 RNA is designated SEQ ID:4472, and is provided hereinbelow with reference to the sequence listing part.

[58950] VGAM1761 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1761 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1761 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[58951] VGAM1761 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1761 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1761 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1761 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1761 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[58952] The complementary binding of VGAM1761 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1761 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1761 host target RNA into VGAM1761 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[58953] It is appreciated that VGAM1761 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1761 host target genes. The mRNA of each one of this plurality of VGAM1761 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1761 RNA, herein designated VGAM RNA, and which when bound by VGAM1761 RNA causes inhibition of translation of respective one or more VGAM1761 host target proteins.

[58954] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1761 gene, herein designated VGAM GENE, on one or more VGAM1761 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[58955] It is yet further appreciated that a function of VGAM1761 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of viral infection by Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). Specific functions, and accordingly

utilities, of VGAM1761 correlate with, and may be deduced from, the identity of the host target genes which VGAM1761 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[58956] Nucleotide sequences of the VGAM1761 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1761 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1761 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1761 are further described hereinbelow with reference to Table 1.

[58957] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1761 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1761 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[58958] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1761 gene, herein designated VGAM is inhibition of expression of VGAM1761 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1761 correlate with, and may be deduced

from, the identity of the target genes which VGAM1761 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[58959] Absent In Melanoma 1 (AIM1, Accession XM\_166300) is a VGAM1761 host target gene. AIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AIM1 BINDING SITE, designated SEQ ID:44115, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58960] A function of VGAM1761 is therefore inhibition of Absent In Melanoma 1 (AIM1, Accession XM\_166300), a gene which interactions with the cytoskeleton. Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AIM1. The function of AIM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM808. Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 6 (CHST6,



Accession NM\_021615) is another VGAM1761 host target gene. CHST6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHST6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST6 BINDING SITE, designated SEQ ID:22247, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58961] Another function of VGAM1761 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 6 (CHST6, Accession NM\_021615). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST6. Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM\_005228) is another VGAM1761 host target gene. EGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of EGFR BINDING SITE, designated SEQ ID:11725, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58962] Another function of VGAM1761 is therefore inhibition of Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM\_005228), a gene which is a receptor for egf, but also for other members of the egf family. Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFR. The function of EGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229. Growth Factor Receptor-bound Protein 14 (GRB14, Accession NM\_004490) is another VGAM1761 host target gene. GRB14 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GRB14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRB14 BINDING SITE, designated SEQ ID:10829, to the nucleotide se-

quence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58963] Another function of VGAM1761 is therefore inhibition of Growth Factor Receptor-bound Protein 14 (GRB14, Accession NM\_004490), a gene which may interact with platelet-derived growth factor receptor (PDGFRB). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRB14. The function of GRB14 has been established by previous studies. Daly et al. (1996) screened a human breast epithelial cell cDNA library with the tyrosine-phosphorylated C terminus of the epidermal growth factor receptor (EGFR) and identified GRB14. GRB14 is a member of the GRB7 family, whose members include the mouse genes Grb7 (OMIM Ref. No. 601522) and Grb10 (OMIM Ref. No. 601523). GRB14, Grb7 and Grb10 all contain a C-terminal SH2 domain and a central domain with similarity to the *C. elegans* protein F10E9.6/mig10. Daly et al. (1996) identified a third region of similarity, an N-terminal motif, P(S/A)IPNPFPEL, which contains the consensus PXXP SH3 binding domain, suggesting that an SH3 protein may bind to these proteins. By sequence analysis, Dong et al. (1997) mapped the GRB14 gene to chromo-

some 2.

[58964] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[58965] Daly, R. J.; Sanderson, G. M.; Janes, P. W.; Sutherland, R. L. : Cloning and characterization of GRB14, a novel member of the GRB7 gene family. J. Biol. Chem. 271: 12502–12510, 1996. ; and

[58966] Dong, L. Q.; Du, H.; Porter, S. G.; Kolakowski, L. F., Jr.; Lee, A. V.; Mandarino, J.; Fan, J.; Yee, D.; Liu, F. : Cloning, chromosome localization, expression, and characterization of.

[58967] Further studies establishing the function and utilities of GRB14 are found in John Hopkins OMIM database record ID 601524, and in cited publications numbered 6532 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. IRTA2 (Accession NM\_031281) is another VGAM1761 host target gene. IRTA2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IRTA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se–

quences of IRTA2 BINDING SITE, designated SEQ ID:25300, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58968] Another function of VGAM1761 is therefore inhibition of IRTA2 (Accession NM\_031281), a gene which binds to the fc region of immunoglobulins gamma low affinity receptor. Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRTA2. The function of IRTA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Promyelocytic Leukemia (PML, Accession NM\_033238) is another VGAM1761 host target gene. PML BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PML, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PML BINDING SITE, designated SEQ ID:27078, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58969] Another function of VGAM1761 is therefore inhibition of

Promyelocytic Leukemia (PML, Accession NM\_033238). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PML. Peanut-like 2 (Drosophila) (PNUTL2, Accession NM\_080415) is another VGAM1761 host target gene. PNUTL2 BINDING SITE1 and PNUTL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PNUTL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PNUTL2 BINDING SITE1 and PNUTL2 BINDING SITE2, designated SEQ ID:27834 and SEQ ID:27838 respectively, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58970] Another function of VGAM1761 is therefore inhibition of Peanut-like 2 (Drosophila) (PNUTL2, Accession NM\_080415), a gene which is involved in cytokinesis. Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PNUTL2. The function of PNUTL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described

hereinabove with reference to VGAM95. Tumor Necrosis Factor (TNF superfamily, member 2) (TNF, Accession XM\_165823) is another VGAM1761 host target gene. TNF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNF BINDING SITE, designated SEQ ID:43770, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58971] Another function of VGAM1761 is therefore inhibition of Tumor Necrosis Factor (TNF superfamily, member 2) (TNF, Accession XM\_165823), a gene which mediates proinflammatory responses and apoptosis. Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNF. The function of TNF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM175. Tripartite Motif-containing 8 (TRIM8, Accession NM\_030912) is another VGAM1761 host target gene. TRIM8 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by TRIM8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM8 BINDING SITE, designated SEQ ID:25182, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58972] Another function of VGAM1761 is therefore inhibition of Tripartite Motif-containing 8 (TRIM8, Accession NM\_030912). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM8. Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM\_017662) is another VGAM1761 host target gene. TRPM6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM6 BINDING SITE, designated SEQ ID:19200, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ



ID:4472.

[58973] Another function of VGAM1761 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM\_017662), a gene which contains a predicted ion channel domain and a protein kinase domain. Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM6. The function of TRPM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173. Ubiquitin Specific Protease 6 (Ure-2 oncogene) (USP6, Accession XM\_165948) is another VGAM1761 host target gene. USP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by USP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP6 BINDING SITE, designated SEQ ID:43811, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58974] Another function of VGAM1761 is therefore inhibition of

Ubiquitin Specific Protease 6 (Tre-2 oncogene) (USP6, Accession XM\_165948), a gene which has an atp-independent isopeptidase activity, cleaving at the carboxyl terminus of the ubiquitin moiety. Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP6. The function of USP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM296.DKFZP434L0718 (Accession NM\_032139) is another VGAM1761 host target gene. DKFZP434L0718 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434L0718, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L0718 BINDING SITE, designated SEQ ID:25822, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58975] Another function of VGAM1761 is therefore inhibition of DKFZP434L0718 (Accession NM\_032139). Accordingly, utilities of VGAM1761 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP434L0718. FLJ14596 (Accession NM\_032809) is another VGAM1761 host target gene. FLJ14596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14596 BINDING SITE, designated SEQ ID:26572, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58976] Another function of VGAM1761 is therefore inhibition of FLJ14596 (Accession NM\_032809). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14596. FLJ21276 (Accession NM\_024633) is another VGAM1761 host target gene. FLJ21276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21276 BINDING SITE, designated SEQ ID:23905, to the nucleotide

sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58977] Another function of VGAM1761 is therefore inhibition of FLJ21276 (Accession NM\_024633). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21276. HSH2 (Accession NM\_032855) is another VGAM1761 host target gene. HSH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSH2 BINDING SITE, designated SEQ ID:26654, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58978] Another function of VGAM1761 is therefore inhibition of HSH2 (Accession NM\_032855). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSH2. KR18 (Accession NM\_033288) is another VGAM1761 host target gene. KR18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by KR18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KR18 BINDING SITE, designated SEQ ID:27114, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58979] Another function of VGAM1761 is therefore inhibition of KR18 (Accession NM\_033288). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KR18. Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010) is another VGAM1761 host target gene. MAP2K4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP2K4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K4 BINDING SITE, designated SEQ ID:8919, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58980] Another function of VGAM1761 is therefore inhibition of

Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM\_003010). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K4. NPD009 (Accession XM\_170795) is another VGAM1761 host target gene. NPD009 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPD009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPD009 BINDING SITE, designated SEQ ID:45563, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58981] Another function of VGAM1761 is therefore inhibition of NPD009 (Accession XM\_170795). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPD009. Triple Homeobox 1 (TIX1, Accession XM\_029734) is another VGAM1761 host target gene. TIX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIX1, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIX1 BINDING SITE, designated SEQ ID:30929, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58982] Another function of VGAM1761 is therefore inhibition of Triple Homeobox 1 (TIX1, Accession XM\_029734). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIX1. LOC129198 (Accession XM\_072197) is another VGAM1761 host target gene. LOC129198 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC129198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129198 BINDING SITE, designated SEQ ID:37464, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58983] Another function of VGAM1761 is therefore inhibition of LOC129198 (Accession XM\_072197). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC129198. LOC143310 (Accession XM\_084485) is another VGAM1761 host target gene. LOC143310 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC143310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143310 BINDING SITE, designated SEQ ID:37609, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58984] Another function of VGAM1761 is therefore inhibition of LOC143310 (Accession XM\_084485). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143310. LOC145453 (Accession XM\_085120) is another VGAM1761 host target gene. LOC145453 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145453 BINDING SITE, designated SEQ ID:37837, to



the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58985] Another function of VGAM1761 is therefore inhibition of LOC145453 (Accession XM\_085120). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145453. LOC150159 (Accession NM\_139173) is another VGAM1761 host target gene. LOC150159 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150159 BINDING SITE, designated SEQ ID:29181, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58986] Another function of VGAM1761 is therefore inhibition of LOC150159 (Accession NM\_139173). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150159. LOC150967 (Accession XM\_087060) is another VGAM1761 host target gene. LOC150967 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC150967, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150967 BINDING SITE, designated SEQ ID:39037, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58987] Another function of VGAM1761 is therefore inhibition of LOC150967 (Accession XM\_087060). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150967. LOC152345 (Accession XM\_087442) is another VGAM1761 host target gene. LOC152345 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152345, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152345 BINDING SITE, designated SEQ ID:39267, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58988] Another function of VGAM1761 is therefore inhibition of LOC152345 (Accession XM\_087442). Accordingly, utilities

of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152345. LOC168576 (Accession XM\_095191) is another VGAM1761 host target gene. LOC168576 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC168576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168576 BINDING SITE, designated SEQ ID:40253, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58989] Another function of VGAM1761 is therefore inhibition of LOC168576 (Accession XM\_095191). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168576. LOC200312 (Accession XM\_117224) is another VGAM1761 host target gene. LOC200312 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC200312 BINDING SITE, designated SEQ ID:43291, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58990] Another function of VGAM1761 is therefore inhibition of LOC200312 (Accession XM\_117224). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200312. LOC203350 (Accession XM\_117536) is another VGAM1761 host target gene. LOC203350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203350 BINDING SITE, designated SEQ ID:43535, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58991] Another function of VGAM1761 is therefore inhibition of LOC203350 (Accession XM\_117536). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203350. LOC220776 (Accession XM\_043388) is another VGAM1761 host target gene. LOC220776 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC220776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220776 BINDING SITE, designated SEQ ID:33936, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58992] Another function of VGAM1761 is therefore inhibition of LOC220776 (Accession XM\_043388). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220776. LOC257551 (Accession XM\_175158) is another VGAM1761 host target gene. LOC257551 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC257551, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257551 BINDING SITE, designated SEQ ID:46644, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58993] Another function of VGAM1761 is therefore inhibition of

LOC257551 (Accession XM\_175158). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257551. LOC257601 (Accession XM\_175231) is another VGAM1761 host target gene. LOC257601 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257601, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257601 BINDING SITE, designated SEQ ID:46695, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58994] Another function of VGAM1761 is therefore inhibition of LOC257601 (Accession XM\_175231). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257601. LOC91585 (Accession XM\_039395) is another VGAM1761 host target gene. LOC91585 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91585, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC91585 BINDING SITE, designated SEQ ID:33077, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58995] Another function of VGAM1761 is therefore inhibition of LOC91585 (Accession XM\_039395). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91585. LOC93624 (Accession XM\_052624) is another VGAM1761 host target gene. LOC93624 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93624 BINDING SITE, designated SEQ ID:36016, to the nucleotide sequence of VGAM1761 RNA, herein designated VGAM RNA, also designated SEQ ID:4472.

[58996] Another function of VGAM1761 is therefore inhibition of LOC93624 (Accession XM\_052624). Accordingly, utilities of VGAM1761 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93624. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1762 (VGAM1762) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[58997] VGAM1762 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1762 was detected is described hereinabove with reference to Figs. 1–8.

[58998] VGAM1762 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV–2). VGAM1762 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[58999] VGAM1762 gene encodes a VGAM1762 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1762 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1762 precursor RNA is designated SEQ ID:1748, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence



SEQ ID:1748 is located at position 2442 relative to the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2).

- [59000] VGAM1762 precursor RNA folds onto itself, forming VGAM1762 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [59001] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1762 folded precursor RNA into VGAM1762 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1762 RNA is designated SEQ ID:4473, and is provided hereinbelow with reference to the sequence listing part.

[59002] VGAM1762 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1762 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1762 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[59003] VGAM1762 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1762 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1762 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1762 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1762 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59004] The complementary binding of VGAM1762 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1762 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1762 host target RNA into VGAM1762 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59005] It is appreciated that VGAM1762 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1762 host target genes. The mRNA of each one of this plurality of VGAM1762 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1762 RNA, herein designated VGAM RNA, and which when bound by VGAM1762 RNA causes

inhibition of translation of respective one or more VGAM1762 host target proteins.

[59006] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1762 gene, herein designated VGAM GENE, on one or more VGAM1762 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59007] It is yet further appreciated that a function of VGAM1762 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1762 include diagnosis, prevention and

treatment of viral infection by Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). Specific functions, and accordingly utilities, of VGAM1762 correlate with, and may be deduced from, the identity of the host target genes which VGAM1762 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59008] Nucleotide sequences of the VGAM1762 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1762 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1762 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1762 are further described hereinbelow with reference to Table 1.

[59009] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1762 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1762 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59010] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1762 gene, herein designated VGAM is inhibition of expression of VGAM1762 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1762 correlate with, and may be deduced from, the identity of the target genes which VGAM1762 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59011] Adrenergic, Beta-3-, Receptor (ADRB3, Accession NM\_000025) is a VGAM1762 host target gene. ADRB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADRB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADRB3 BINDING SITE, designated SEQ ID:5460, to the nucleotide sequence of VGAM1762 RNA, herein designated VGAM RNA, also designated SEQ ID:4473.

[59012] A function of VGAM1762 is therefore inhibition of Adrenergic, Beta-3-, Receptor (ADRB3, Accession NM\_000025), a gene which stimulates adenylyl cyclase activity and regulates lipolysis. Accordingly, utilities of VGAM1762 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADRB3. The function of ADRB3 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM179. Contactin Associated Protein-like 2 (CNTNAP2, Accession NM\_014141) is another VGAM1762 host target gene. CNTNAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNTNAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNTNAP2 BINDING SITE, designated SEQ ID:15419, to the nucleotide sequence of VGAM1762 RNA, herein designated VGAM RNA, also designated SEQ ID:4473.

[59013] Another function of VGAM1762 is therefore inhibition of Contactin Associated Protein-like 2 (CNTNAP2, Accession NM\_014141). Accordingly, utilities of VGAM1762 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNTNAP2. FLJ22746 (Accession NM\_024785) is another VGAM1762 host target gene. FLJ22746 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22746, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of FLJ22746 BINDING SITE, designated SEQ ID:24165, to the nucleotide sequence of VGAM1762 RNA, herein designated VGAM RNA, also designated SEQ ID:4473.

[59014] Another function of VGAM1762 is therefore inhibition of FLJ22746 (Accession NM\_024785). Accordingly, utilities of VGAM1762 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22746. SQV7L (Accession XM\_047287) is another VGAM1762 host target gene. SQV7L BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SQV7L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SQV7L BINDING SITE, designated SEQ ID:34933, to the nucleotide sequence of VGAM1762 RNA, herein designated VGAM RNA, also designated SEQ ID:4473.

[59015] Another function of VGAM1762 is therefore inhibition of SQV7L (Accession XM\_047287). Accordingly, utilities of VGAM1762 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SQV7L. Zinc Finger Protein 237 (ZNF237, Accession NM\_014242)



is another VGAM1762 host target gene. ZNF237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF237 BINDING SITE, designated SEQ ID:15505, to the nucleotide sequence of VGAM1762 RNA, herein designated VGAM RNA, also designated SEQ ID:4473.

[59016] Another function of VGAM1762 is therefore inhibition of Zinc Finger Protein 237 (ZNF237, Accession NM\_014242). Accordingly, utilities of VGAM1762 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF237. LOC153688 (Accession XM\_098416) is another VGAM1762 host target gene. LOC153688 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153688 BINDING SITE, designated SEQ ID:41653, to the nucleotide sequence of VGAM1762 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4473.

[59017] Another function of VGAM1762 is therefore inhibition of LOC153688 (Accession XM\_098416). Accordingly, utilities of VGAM1762 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153688. LOC220846 (Accession XM\_165515) is another VGAM1762 host target gene. LOC220846 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220846, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220846 BINDING SITE, designated SEQ ID:43662, to the nucleotide sequence of VGAM1762 RNA, herein designated VGAM RNA, also designated SEQ ID:4473.

[59018] Another function of VGAM1762 is therefore inhibition of LOC220846 (Accession XM\_165515). Accordingly, utilities of VGAM1762 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220846. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1763 (VGAM1763) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59019] VGAM1763 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1763 was detected is described hereinabove with reference to Figs. 1–8.

[59020] VGAM1763 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV–2). VGAM1763 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59021] VGAM1763 gene encodes a VGAM1763 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1763 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1763 precursor RNA is designated SEQ ID:1749, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1749 is located at position 11479 relative to the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV–2).

[59022] VGAM1763 precursor RNA folds onto itself, forming VGAM1763 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59023] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1763 folded precursor RNA into VGAM1763 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1763 RNA is designated SEQ ID:4474, and is provided hereinbelow with reference to the sequence listing part.

[59024] VGAM1763 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1763 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1763 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[59025] VGAM1763 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1763 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1763 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1763 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1763 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59026] The complementary binding of VGAM1763 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1763 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1763 host target RNA into VGAM1763 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59027] It is appreciated that VGAM1763 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1763 host target genes. The mRNA of each one of this plurality of VGAM1763 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1763 RNA, herein designated VGAM RNA, and which when bound by VGAM1763 RNA causes inhibition of translation of respective one or more VGAM1763 host target proteins.

[59028] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1763 gene, herein designated VGAM GENE, on one or more VGAM1763 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59029] It is yet further appreciated that a function of VGAM1763 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of viral infection by Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). Specific functions, and accordingly utilities, of VGAM1763 correlate with, and may be de-

duced from, the identity of the host target genes which VGAM1763 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59030] Nucleotide sequences of the VGAM1763 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1763 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1763 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1763 are further described hereinbelow with reference to Table 1.

[59031] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1763 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1763 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59032] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1763 gene, herein designated VGAM is inhibition of expression of VGAM1763 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1763 correlate with, and may be deduced from, the identity of the target genes which VGAM1763



binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59033] Corticotropin Releasing Hormone Receptor 2 (CRHR2, Accession NM\_001883) is a VGAM1763 host target gene. CRHR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRHR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRHR2 BINDING SITE, designated SEQ ID:7613, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59034] A function of VGAM1763 is therefore inhibition of Corticotropin Releasing Hormone Receptor 2 (CRHR2, Accession NM\_001883), a gene which is a corticotropin releasing factor receptor type II. Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRHR2. The function of CRHR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM737. Dual Specificity Phosphatase 6 (DUSP6, Ac-

cession XM\_038308) is another VGAM1763 host target gene. DUSP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DUSP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP6 BINDING SITE, designated SEQ ID:32810, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59035] Another function of VGAM1763 is therefore inhibition of Dual Specificity Phosphatase 6 (DUSP6, Accession XM\_038308), a gene which inactivates map kinases. Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DUSP6. The function of DUSP6 has been established by previous studies. Members of the mitogen-activated protein (MAP) kinase family play a pivotal role in cellular signal transduction. The dual-specificity phosphatases can reverse MAP kinase activation by dephosphorylating critical phosphotyrosine and phosphothreonine residues. Muda et al. (1996) identified rat superior cervical ganglion cDNAs encoding 2 dual-specificity phos-

phatases that they designated MKP3 and MKPX (OMIM Ref. No. 602749). Northern analysis revealed that nerve growth factor (see OMIM Ref. No. 162030) induced MKP3 expression in PC12 cells. By in situ hybridization, Muda et al. (1996) showed that metrazole-stimulated seizure activity induced MKP3 expression, rapidly and transiently, in specific regions of the brain. When expressed in mammalian cells, MKP3 blocked both the phosphorylation and enzymatic activation of the MAP kinase ERK2 (OMIM Ref. No. 176948) by mitogens. Muda et al. (1996) concluded that MKP3 may play an important and specific role in regulating MAP kinase activities. Groom et al. (1996) identified cDNAs encoding the human MKP3 and MKPX homologs, which they called PYST1 and PYST2, respectively. Like other dual-specificity phosphatases, the N-terminal region of the predicted 381-amino acid PYST1 protein has 2 domains with significant homology to CDC25 (OMIM Ref. No. 157680). By immunofluorescence of mammalian cells expressing epitope-tagged PYST1, Groom et al. (1996) showed that the protein is localized to the cytoplasm. They found that PYST1 dephosphorylated and inactivated MAP kinase in vitro and in vivo, but displayed very low activity towards the related stress-activated pro-

tein kinases (SAPKs; OMIM Ref. No. 601158). When expressed in mammalian cells, PYST1 formed a physical complex with endogenous MAP kinase. Northern analysis revealed that PYST1 is expressed as a 3-kb mRNA in a variety of tissues, with the highest levels in heart and pancreas. By RT-PCR, Furukawa et al. (1998) found that DUSP6 was expressed as 2 differently sized transcripts in all tissues tested.

[59036] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59037] Groom, L. A.; Sneddon, A. A.; Alessi, D. R.; Dowd, S.; Keyse, S. M. : Differential regulation of the MAP, SAP and RK/p38 kinases by Pyst1, a novel cytosolic dual-specificity phosphatase. EMBO J. 15: 3621-3632, 1996. ; and

[59038] Muda, M.; Boschert, U.; Dickinson, R.; Martinou, J.-C.; Martinou, I.; Camps, M.; Schlegel, W.; Arkinstall, S. : MKP-3, a novel cytosolic protein-tyrosine phosphatase that exemplifies a.

[59039] Further studies establishing the function and utilities of DUSP6 are found in John Hopkins OMIM database record ID 602748, and in cited publications numbered 2410-241 and 2409 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Low Density Lipoprotein Receptor-related Protein 8, Apolipoprotein E Receptor (LRP8, Accession NM\_033300) is another VGAM1763 host target gene. LRP8 BINDING SITE1 and LRP8 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LRP8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP8 BINDING SITE1 and LRP8 BINDING SITE2, designated SEQ ID:27130 and SEQ ID:11006 respectively, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59040] Another function of VGAM1763 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 8, Apolipoprotein E Receptor (LRP8, Accession NM\_033300), a gene which binds vldl and transports it into cells by endocytosis. Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP8. The function of LRP8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Cell Ad-

hesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM\_006614) is another VGAM1763 host target gene. CHL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHL1 BINDING SITE, designated SEQ ID:13398, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59041] Another function of VGAM1763 is therefore inhibition of Cell Adhesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM\_006614). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHL1. DJ167A19.1 (Accession NM\_018982) is another VGAM1763 host target gene. DJ167A19.1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ167A19.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of DJ167A19.1 BINDING SITE, designated SEQ ID:21051, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59042] Another function of VGAM1763 is therefore inhibition of DJ167A19.1 (Accession NM\_018982). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ167A19.1. FLJ22054 (Accession XM\_170478) is another VGAM1763 host target gene. FLJ22054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22054 BINDING SITE, designated SEQ ID:45318, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59043] Another function of VGAM1763 is therefore inhibition of FLJ22054 (Accession XM\_170478). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22054. GFR (Accession NM\_012294) is another VGAM1763 host target gene. GFR BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by GFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFR BINDING SITE, designated SEQ ID:14643, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59044] Another function of VGAM1763 is therefore inhibition of GFR (Accession NM\_012294). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFR. Histone Deacetylase 11 (HDAC11, Accession NM\_024827) is another VGAM1763 host target gene. HDAC11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HDAC11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC11 BINDING SITE, designated SEQ ID:24218, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59045] Another function of VGAM1763 is therefore inhibition of



Histone Deacetylase 11 (HDAC11, Accession NM\_024827). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC11. KIAA0415 (Accession XM\_166527) is another VGAM1763 host target gene. KIAA0415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0415 BINDING SITE, designated SEQ ID:44475, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59046] Another function of VGAM1763 is therefore inhibition of KIAA0415 (Accession XM\_166527). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0415. KIAA0978 (Accession XM\_047013) is another VGAM1763 host target gene. KIAA0978 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0978, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0978 BINDING SITE, designated SEQ ID:34888, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59047] Another function of VGAM1763 is therefore inhibition of KIAA0978 (Accession XM\_047013). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0978. KIAA1042 (Accession NM\_014965) is another VGAM1763 host target gene. KIAA1042 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1042 BINDING SITE, designated SEQ ID:17354, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59048] Another function of VGAM1763 is therefore inhibition of KIAA1042 (Accession NM\_014965). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1042. KIAA1045 (Accession XM\_048592) is another VGAM1763 host target gene. KIAA1045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1045 BINDING SITE, designated SEQ ID:35201, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59049] Another function of VGAM1763 is therefore inhibition of KIAA1045 (Accession XM\_048592). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1045. MGC12760 (Accession NM\_032723) is another VGAM1763 host target gene. MGC12760 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12760, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12760 BINDING SITE, designated SEQ ID:26451, to the nucleotide sequence of VGAM1763 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4474.

[59050] Another function of VGAM1763 is therefore inhibition of MGC12760 (Accession NM\_032723). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12760. PRO0800 (Accession NM\_018592) is another VGAM1763 host target gene. PRO0800 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0800 BINDING SITE, designated SEQ ID:20672, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59051] Another function of VGAM1763 is therefore inhibition of PRO0800 (Accession NM\_018592). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0800. SQV7L (Accession XM\_047287) is another VGAM1763 host target gene. SQV7L BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SQV7L, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SQV7L BINDING SITE, designated SEQ ID:34934, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59052] Another function of VGAM1763 is therefore inhibition of SQV7L (Accession XM\_047287). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SQV7L. LOC170082 (Accession XM\_093092) is another VGAM1763 host target gene. LOC170082 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170082 BINDING SITE, designated SEQ ID:40171, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59053] Another function of VGAM1763 is therefore inhibition of LOC170082 (Accession XM\_093092). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC170082. LOC221687 (Accession XM\_166423) is another VGAM1763 host target gene. LOC221687 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221687 BINDING SITE, designated SEQ ID:44308, to the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59054] Another function of VGAM1763 is therefore inhibition of LOC221687 (Accession XM\_166423). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221687. LOC255862 (Accession XM\_170505) is another VGAM1763 host target gene. LOC255862 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC255862, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255862 BINDING SITE, designated SEQ ID:45343, to

the nucleotide sequence of VGAM1763 RNA, herein designated VGAM RNA, also designated SEQ ID:4474.

[59055] Another function of VGAM1763 is therefore inhibition of LOC255862 (Accession XM\_170505). Accordingly, utilities of VGAM1763 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255862. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1764 (VGAM1764) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59056] VGAM1764 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1764 was detected is described hereinabove with reference to Figs. 1–8.

[59057] VGAM1764 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). VGAM1764 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59058] VGAM1764 gene encodes a VGAM1764 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1764 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1764 precursor RNA is designated SEQ ID:1750, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1750 is located at position 3861 relative to the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2).

[59059] VGAM1764 precursor RNA folds onto itself, forming VGAM1764 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59060] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1764 folded precursor RNA into VGAM1764 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1764 RNA is designated SEQ ID:4475, and is provided hereinbelow with reference to the sequence listing part.

[59061] VGAM1764 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1764 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1764 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59062] VGAM1764 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1764 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1764 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1764 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1764 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59063] The complementary binding of VGAM1764 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1764 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1764 host target RNA into VGAM1764 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59064] It is appreciated that VGAM1764 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1764 host target genes. The mRNA of each one of this plurality of VGAM1764 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1764 RNA, herein designated VGAM RNA, and which when bound by VGAM1764 RNA causes inhibition of translation of respective one or more VGAM1764 host target proteins.

[59065] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1764 gene, herein designated VGAM GENE, on one or more VGAM1764 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[59066] It is yet further appreciated that a function of VGAM1764 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of viral infection by Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). Specific functions, and accordingly utilities, of VGAM1764 correlate with, and may be deduced from, the identity of the host target genes which VGAM1764 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59067] Nucleotide sequences of the VGAM1764 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1764 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1764 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1764 are further described hereinbelow with reference to Table 1.

[59068] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1764 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1764 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59069] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1764 gene, herein designated VGAM is inhibition of expression of VGAM1764 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1764 correlate with, and may be deduced from, the identity of the target genes which VGAM1764 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59070] EGF-like-domain, Multiple 5 (EGFL5, Accession XM\_098838) is a VGAM1764 host target gene. EGFL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL5 BINDING SITE, designated SEQ ID:41877, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59071] A function of VGAM1764 is therefore inhibition of EGF-

like-domain, Multiple 5 (EGFL5, Accession XM\_098838). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL5. Protocadherin Beta 16 (PCDHB16, Accession NM\_020957) is another VGAM1764 host target gene. PCDHB16 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PCDHB16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB16 BINDING SITE, designated SEQ ID:21948, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59072] Another function of VGAM1764 is therefore inhibition of Protocadherin Beta 16 (PCDHB16, Accession NM\_020957), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHB16. The function of PCDHB16 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM931.Tripartite Motif-containing 14 (TRIM14, Accession NM\_014788) is another VGAM1764 host target gene. TRIM14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM14 BINDING SITE, designated SEQ ID:16669, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59073] Another function of VGAM1764 is therefore inhibition of Tripartite Motif-containing 14 (TRIM14, Accession NM\_014788), a gene which is composed of 3 zinc-binding domains and is involved in development and cell growth. Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM14. The function of TRIM14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180.Cyclin E2 (CCNE2, Accession NM\_004702) is another VGAM1764 host target gene. CCNE2 BINDING SITE1 and CCNE2 BIND-

ING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCNE2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNE2 BINDING SITE1 and CCNE2 BINDING SITE2, designated SEQ ID:11048 and SEQ ID:27709 respectively, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59074] Another function of VGAM1764 is therefore inhibition of Cyclin E2 (CCNE2, Accession NM\_004702). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNE2. DKFZP566F2124 (Accession NM\_015630) is another VGAM1764 host target gene. DKFZP566F2124 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566F2124, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566F2124 BINDING SITE, designated SEQ ID:17889, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also des-



ignated SEQ ID:4475.

[59075] Another function of VGAM1764 is therefore inhibition of DKFZP566F2124 (Accession NM\_015630). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566F2124. Ecotropic Viral Integration Site 5 (EVI5, Accession NM\_005665) is another VGAM1764 host target gene. EVI5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EVI5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVI5 BINDING SITE, designated SEQ ID:12214, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59076] Another function of VGAM1764 is therefore inhibition of Ecotropic Viral Integration Site 5 (EVI5, Accession NM\_005665). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVI5. KIAA0368 (Accession XM\_036708) is another VGAM1764 host target gene. KIAA0368 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by KIAA0368, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0368 BINDING SITE, designated SEQ ID:32489, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59077] Another function of VGAM1764 is therefore inhibition of KIAA0368 (Accession XM\_036708). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0368. KIAA1508 (Accession XM\_030209) is another VGAM1764 host target gene. KIAA1508 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1508 BINDING SITE, designated SEQ ID:30996, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59078] Another function of VGAM1764 is therefore inhibition of

KIAA1508 (Accession XM\_030209). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1508. KIAA1535 (Accession XM\_086565) is another VGAM1764 host target gene. KIAA1535 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1535 BINDING SITE, designated SEQ ID:38768, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59079] Another function of VGAM1764 is therefore inhibition of KIAA1535 (Accession XM\_086565). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1535. MFN2 (Accession NM\_014874) is another VGAM1764 host target gene. MFN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MFN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of MFN2 BINDING SITE, designated SEQ ID:17012, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59080] Another function of VGAM1764 is therefore inhibition of MFN2 (Accession NM\_014874). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MFN2. Nuclear Receptor Subfamily 6, Group A, Member 1 (NR6A1, Accession NM\_001489) is another VGAM1764 host target gene. NR6A1 BINDING SITE1 through NR6A1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NR6A1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR6A1 BINDING SITE1 through NR6A1 BINDING SITE3, designated SEQ ID:7230, SEQ ID:27178 and SEQ ID:27184 respectively, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59081] Another function of VGAM1764 is therefore inhibition of Nuclear Receptor Subfamily 6, Group A, Member 1

(NR6A1, Accession NM\_001489). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR6A1. NY-REN-60 (Accession XM\_040506) is another VGAM1764 host target gene. NY-REN-60 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NY-REN-60, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-60 BINDING SITE, designated SEQ ID:33319, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59082] Another function of VGAM1764 is therefore inhibition of NY-REN-60 (Accession XM\_040506). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-60. Paternally Expressed 10 (PEG10, Accession NM\_015068) is another VGAM1764 host target gene. PEG10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEG10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of PEG10 BINDING SITE, designated SEQ ID:17431, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59083] Another function of VGAM1764 is therefore inhibition of Paternally Expressed 10 (PEG10, Accession NM\_015068). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEG10. Pellino Homolog 2 (Drosophila) (PELI2, Accession NM\_021255) is another VGAM1764 host target gene. PELI2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PELI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PELI2 BINDING SITE, designated SEQ ID:22228, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59084] Another function of VGAM1764 is therefore inhibition of Pellino Homolog 2 (Drosophila) (PELI2, Accession NM\_021255). Accordingly, utilities of VGAM1764 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with PELI2. PRO2133 (Accession NM\_018619) is another VGAM1764 host target gene.

PRO2133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2133 BINDING SITE, designated SEQ ID:20691, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59085] Another function of VGAM1764 is therefore inhibition of PRO2133 (Accession NM\_018619). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2133. Sulfotransferase Family, Cytosolic, 1C, Member 2 (SULT1C2, Accession NM\_006588) is another VGAM1764 host target gene. SULT1C2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SULT1C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of SULT1C2 BINDING SITE, designated SEQ ID:13352, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59086] Another function of VGAM1764 is therefore inhibition of Sulfotransferase Family, Cytosolic, 1C, Member 2 (SULT1C2, Accession NM\_006588). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SULT1C2. LOC143879 (Accession XM\_084666) is another VGAM1764 host target gene. LOC143879 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143879, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143879 BINDING SITE, designated SEQ ID:37661, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59087] Another function of VGAM1764 is therefore inhibition of LOC143879 (Accession XM\_084666). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC143879. LOC154007 (Accession XM\_087824) is another VGAM1764 host target gene. LOC154007 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154007 BINDING SITE, designated SEQ ID:39453, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59088] Another function of VGAM1764 is therefore inhibition of LOC154007 (Accession XM\_087824). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154007. LOC203636 (Accession XM\_114868) is another VGAM1764 host target gene. LOC203636 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203636, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203636 BINDING SITE, designated SEQ ID:43076, to the nucleotide sequence of VGAM1764 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4475.

[59089] Another function of VGAM1764 is therefore inhibition of LOC203636 (Accession XM\_114868). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203636. LOC221477 (Accession XM\_166397) is another VGAM1764 host target gene. LOC221477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221477 BINDING SITE, designated SEQ ID:44252, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59090] Another function of VGAM1764 is therefore inhibition of LOC221477 (Accession XM\_166397). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221477. LOC51336 (Accession NM\_016646) is another VGAM1764 host target gene. LOC51336 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51336, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51336 BINDING SITE, designated SEQ ID:18756, to the nucleotide sequence of VGAM1764 RNA, herein designated VGAM RNA, also designated SEQ ID:4475.

[59091] Another function of VGAM1764 is therefore inhibition of LOC51336 (Accession NM\_016646). Accordingly, utilities of VGAM1764 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51336. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1765 (VGAM1765) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59092] VGAM1765 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1765 was detected is described hereinabove with reference to Figs. 1-8.

[59093] VGAM1765 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Viral Diarrhea

Virus Genotype 2 (BVDV-2). VGAM1765 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59094] VGAM1765 gene encodes a VGAM1765 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1765 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1765 precursor RNA is designated SEQ ID:1751, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1751 is located at position 9624 relative to the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2).

[59095] VGAM1765 precursor RNA folds onto itself, forming VGAM1765 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59096] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1765 folded precursor RNA into VGAM1765 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1765 RNA is designated SEQ ID:4476, and is provided hereinbelow with reference to the sequence listing part.

[59097] VGAM1765 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1765 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1765 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59098] VGAM1765 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1765 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1765 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1765 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1765 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59099] The complementary binding of VGAM1765 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1765 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1765

host target RNA into VGAM1765 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59100] It is appreciated that VGAM1765 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1765 host target genes. The mRNA of each one of this plurality of VGAM1765 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1765 RNA, herein designated VGAM RNA, and which when bound by VGAM1765 RNA causes inhibition of translation of respective one or more VGAM1765 host target proteins.

[59101] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1765 gene, herein designated VGAM GENE, on one or more VGAM1765 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59102] It is yet further appreciated that a function of VGAM1765 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1765 include diagnosis, prevention and treatment of viral infection by Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). Specific functions, and accordingly utilities, of VGAM1765 correlate with, and may be deduced from, the identity of the host target genes which VGAM1765 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59103] Nucleotide sequences of the VGAM1765 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1765 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1765 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1765 are further



described hereinbelow with reference to Table 1.

[59104] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1765 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1765 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59105] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1765 gene, herein designated VGAM is inhibition of expression of VGAM1765 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1765 correlate with, and may be deduced from, the identity of the target genes which VGAM1765 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59106] Cyclin D1 (PRAD1: parathyroid adenomatosis 1) (CCND1, Accession NM\_053056) is a VGAM1765 host target gene. CCND1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of CCND1 BINDING SITE, designated SEQ ID:27597, to the nucleotide sequence of VGAM1765 RNA, herein designated VGAM RNA, also designated SEQ ID:4476.

[59107] A function of VGAM1765 is therefore inhibition of Cyclin D1 (PRAD1: parathyroid adenomatosis 1) (CCND1, Accession NM\_053056), a gene which is involved in the control of cell cycle and is required for Schwann cell proliferation to proceed normally during Wallerian degeneration. Accordingly, utilities of VGAM1765 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND1. The function of CCND1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM220.LOC157280 (Accession XM\_058301) is another VGAM1765 host target gene. LOC157280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157280 BINDING SITE, designated SEQ ID:36591, to the nucleotide sequence of

VGAM1765 RNA, herein designated VGAM RNA, also designated SEQ ID:4476.

[59108] Another function of VGAM1765 is therefore inhibition of LOC157280 (Accession XM\_058301). Accordingly, utilities of VGAM1765 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157280. LOC255448 (Accession XM\_170623) is another VGAM1765 host target gene. LOC255448 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255448, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255448 BINDING SITE, designated SEQ ID:45401, to the nucleotide sequence of VGAM1765 RNA, herein designated VGAM RNA, also designated SEQ ID:4476.

[59109] Another function of VGAM1765 is therefore inhibition of LOC255448 (Accession XM\_170623). Accordingly, utilities of VGAM1765 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255448. LOC92661 (Accession XM\_046465) is another VGAM1765 host target gene. LOC92661 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC92661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92661 BINDING SITE, designated SEQ ID:34720, to the nucleotide sequence of VGAM1765 RNA, herein designated VGAM RNA, also designated SEQ ID:4476.

[59110] Another function of VGAM1765 is therefore inhibition of LOC92661 (Accession XM\_046465). Accordingly, utilities of VGAM1765 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92661. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1766 (VGAM1766) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59111] VGAM1766 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1766 was detected is described hereinabove with reference to Figs. 1-8.

[59112] VGAM1766 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). VGAM1766 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59113] VGAM1766 gene encodes a VGAM1766 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1766 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1766 precursor RNA is designated SEQ ID:1752, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1752 is located at position 5325 relative to the genome of Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2).

[59114] VGAM1766 precursor RNA folds onto itself, forming VGAM1766 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[59115] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1766 folded precursor RNA into VGAM1766 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1766 RNA is designated SEQ ID:4477, and is provided hereinbelow with reference to the sequence listing part.

[59116] VGAM1766 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1766 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1766 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59117] VGAM1766 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1766 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1766 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1766 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1766 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[59118] The complementary binding of VGAM1766 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1766 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1766 host target RNA into VGAM1766 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59119] It is appreciated that VGAM1766 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1766 host target genes. The mRNA of each one of this plurality of VGAM1766 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1766 RNA, herein designated VGAM RNA, and which when bound by VGAM1766 RNA causes inhibition of translation of respective one or more VGAM1766 host target proteins.

[59120] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1766 gene, herein designated VGAM GENE, on one or more VGAM1766 host target gene, herein designated



VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59121] It is yet further appreciated that a function of VGAM1766 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of viral infection by Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). Specific functions, and accordingly utilities, of VGAM1766 correlate with, and may be deduced from, the identity of the host target genes which VGAM1766 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59122] Nucleotide sequences of the VGAM1766 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1766 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1766 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1766 are further  
described hereinbelow with reference to Table 1.

[59123] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1766 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1766 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[59124] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1766 gene, herein designated VGAM is  
inhibition of expression of VGAM1766 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1766 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1766  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[59125] Serine/arginine Repetitive Matrix 1 (SRRM1, Accession  
NM\_005839) is a VGAM1766 host target gene. SRRM1

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRRM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRRM1 BINDING SITE, designated SEQ ID:12451, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59126] A function of VGAM1766 is therefore inhibition of Serine/arginine Repetitive Matrix 1 (SRRM1, Accession NM\_005839). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRRM1. Serine/threonine Kinase 38 (STK38, Accession NM\_007271) is another VGAM1766 host target gene. STK38 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STK38, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK38 BINDING SITE, designated SEQ ID:14133, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59127] Another function of VGAM1766 is therefore inhibition of Serine/threonine Kinase 38 (STK38, Accession NM\_007271). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK38. Ras Homolog Gene Family, Member U (ARHU, Accession NM\_021205) is another VGAM1766 host target gene. ARHU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHU BINDING SITE, designated SEQ ID:22183, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59128] Another function of VGAM1766 is therefore inhibition of Ras Homolog Gene Family, Member U (ARHU, Accession NM\_021205). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHU. Thioesterase, Adipose Associated (THEA, Accession XM\_038922) is another VGAM1766 host target gene. THEA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by THEA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THEA BINDING SITE, designated SEQ ID:32951, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59129] Another function of VGAM1766 is therefore inhibition of Thioesterase, Adipose Associated (THEA, Accession XM\_038922). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THEA. Zinc Finger Protein 347 (ZNF347, Accession NM\_032584) is another VGAM1766 host target gene. ZNF347 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF347, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF347 BINDING SITE, designated SEQ ID:26318, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59130] Another function of VGAM1766 is therefore inhibition of

Zinc Finger Protein 347 (ZNF347, Accession NM\_032584). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF347. LOC131873 (Accession XM\_067585) is another VGAM1766 host target gene. LOC131873 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC131873, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131873 BINDING SITE, designated SEQ ID:37364, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59131] Another function of VGAM1766 is therefore inhibition of LOC131873 (Accession XM\_067585). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131873. LOC143465 (Accession XM\_096430) is another VGAM1766 host target gene. LOC143465 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC143465, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143465 BINDING SITE, designated SEQ ID:40359, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59132] Another function of VGAM1766 is therefore inhibition of LOC143465 (Accession XM\_096430). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143465. LOC158927 (Accession XM\_099004) is another VGAM1766 host target gene. LOC158927 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158927, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158927 BINDING SITE, designated SEQ ID:42041, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59133] Another function of VGAM1766 is therefore inhibition of LOC158927 (Accession XM\_099004). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC158927. LOC221495 (Accession XM\_168136) is another VGAM1766 host target gene. LOC221495 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221495 BINDING SITE, designated SEQ ID:45054, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59134] Another function of VGAM1766 is therefore inhibition of LOC221495 (Accession XM\_168136). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221495. LOC257319 (Accession XM\_171049) is another VGAM1766 host target gene. LOC257319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257319 BINDING SITE, designated SEQ ID:45832, to the nucleotide sequence of VGAM1766 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4477.

[59135] Another function of VGAM1766 is therefore inhibition of LOC257319 (Accession XM\_171049). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257319. LOC51031 (Accession NM\_016080) is another VGAM1766 host target gene. LOC51031 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51031 BINDING SITE, designated SEQ ID:18153, to the nucleotide sequence of VGAM1766 RNA, herein designated VGAM RNA, also designated SEQ ID:4477.

[59136] Another function of VGAM1766 is therefore inhibition of LOC51031 (Accession NM\_016080). Accordingly, utilities of VGAM1766 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51031. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1767 (VGAM1767) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59137] VGAM1767 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1767 was detected is described hereinabove with reference to Figs. 1–8.

[59138] VGAM1767 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM1767 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59139] VGAM1767 gene encodes a VGAM1767 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1767 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1767 precursor RNA is designated SEQ ID:1753, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1753 is located at position 1407 relative to the genome of Rabbit Fibroma Virus.

[59140] VGAM1767 precursor RNA folds onto itself, forming

VGAM1767 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59141] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1767 folded precursor RNA into VGAM1767 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1767 RNA is designated SEQ ID:4478, and is provided hereinbelow with reference to the sequence listing part.

[59142] VGAM1767 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1767 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1767 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59143] VGAM1767 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1767 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1767 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1767 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1767 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59144] The complementary binding of VGAM1767 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1767 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1767 host target RNA into VGAM1767 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59145] It is appreciated that VGAM1767 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1767 host target genes. The mRNA of each one of this plurality of VGAM1767 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1767 RNA, herein designated VGAM RNA, and which when bound by VGAM1767 RNA causes inhibition of translation of respective one or more VGAM1767 host target proteins.

[59146] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1767 gene, herein designated VGAM GENE, on one or more VGAM1767 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59147] It is yet further appreciated that a function of VGAM1767 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM1767 correlate with, and may be deduced from, the identity of the host target genes which VGAM1767 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[59148] Nucleotide sequences of the VGAM1767 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1767 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1767 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1767 are further described hereinbelow with reference to Table 1.

[59149] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1767 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1767 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59150] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1767 gene, herein designated VGAM is inhibition of expression of VGAM1767 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1767 correlate with, and may be deduced from, the identity of the target genes which VGAM1767 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[59151] Cystic Fibrosis Transmembrane Conductance Regulator, ATP-binding Cassette (sub-family C, member 7) (CFTR, Accession NM\_000492) is a VGAM1767 host target gene. CFTR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CFTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CFTR BINDING SITE, designated SEQ ID:6102, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59152] A function of VGAM1767 is therefore inhibition of Cystic Fibrosis Transmembrane Conductance Regulator, ATP-binding Cassette (sub-family C, member 7) (CFTR, Accession NM\_000492). Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CFTR. Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440) is another VGAM1767 host target gene. EXTL3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EXTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL3 BINDING SITE, designated SEQ ID:7167, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59153] Another function of VGAM1767 is therefore inhibition of Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440), a gene which is a member of the multiple exostoses gene family. Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL3. The function of EXTL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 3 (GNAI3, Accession NM\_006496) is another VGAM1767 host target gene. GNAI3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAI3 BINDING SITE, designated SEQ

ID:13241, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59154] Another function of VGAM1767 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 3 (GNAI3, Accession NM\_006496), a gene which stimulates receptor regulated K<sup>+</sup>-channels. Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAI3. The function of GNAI3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM45. Formin Binding Protein 3 (FNBP3, Accession XM\_087118) is another VGAM1767 host target gene. FNBP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FNBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FNBP3 BINDING SITE, designated SEQ ID:39074, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ

ID:4478.

[59155] Another function of VGAM1767 is therefore inhibition of Formin Binding Protein 3 (FNBP3, Accession XM\_087118). Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FNBP3. KIAA0781 (Accession XM\_041314) is another VGAM1767 host target gene. KIAA0781 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0781, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0781 BINDING SITE, designated SEQ ID:33501, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59156] Another function of VGAM1767 is therefore inhibition of KIAA0781 (Accession XM\_041314). Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0781. KIAA1715 (Accession XM\_042834) is another VGAM1767 host target gene. KIAA1715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1715 BINDING SITE, designated SEQ ID:33793, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59157] Another function of VGAM1767 is therefore inhibition of KIAA1715 (Accession XM\_042834). Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1715. PIP3-E (Accession XM\_039749) is another VGAM1767 host target gene. PIP3-E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP3-E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP3-E BINDING SITE, designated SEQ ID:33179, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59158] Another function of VGAM1767 is therefore inhibition of PIP3-E (Accession XM\_039749). Accordingly, utilities of

VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP3-E. Splicing Factor, Arginine/serine-rich 5 (SFRS5, Accession NM\_006925) is another VGAM1767 host target gene.

SFRS5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SFRS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS5 BINDING SITE, designated SEQ ID:13805, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59159] Another function of VGAM1767 is therefore inhibition of Splicing Factor, Arginine/serine-rich 5 (SFRS5, Accession NM\_006925). Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS5. LOC160414 (Accession XM\_100898) is another VGAM1767 host target gene. LOC160414 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC160414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC160414 BINDING SITE, designated SEQ ID:42104, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59160] Another function of VGAM1767 is therefore inhibition of LOC160414 (Accession XM\_100898). Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160414. LOC170217 (Accession XM\_093185) is another VGAM1767 host target gene. LOC170217 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC170217, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170217 BINDING SITE, designated SEQ ID:40179, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59161] Another function of VGAM1767 is therefore inhibition of LOC170217 (Accession XM\_093185). Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170217. LOC170218 (Accession XM\_093186) is an-

other VGAM1767 host target gene. LOC170218 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC170218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170218 BINDING SITE, designated SEQ ID:40181, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59162] Another function of VGAM1767 is therefore inhibition of LOC170218 (Accession XM\_093186). Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170218. LOC206887 (Accession XM\_116781) is another VGAM1767 host target gene. LOC206887 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC206887, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC206887 BINDING SITE, designated SEQ ID:43125, to the nucleotide sequence of VGAM1767 RNA, herein designated VGAM RNA, also designated SEQ ID:4478.

[59163] Another function of VGAM1767 is therefore inhibition of LOC206887 (Accession XM\_116781). Accordingly, utilities of VGAM1767 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC206887. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1768 (VGAM1768) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59164] VGAM1768 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1768 was detected is described hereinabove with reference to Figs. 1–8.

[59165] VGAM1768 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM1768 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59166] VGAM1768 gene encodes a VGAM1768 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,



VGAM1768 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1768 precursor RNA is designated SEQ ID:1754, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1754 is located at position 431 relative to the genome of Rabbit Fibroma Virus.

[59167] VGAM1768 precursor RNA folds onto itself, forming VGAM1768 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59168] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1768 folded precursor RNA into VGAM1768 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1768 RNA is designated SEQ ID:4479, and is provided hereinbelow with reference to the sequence listing part.

[59169] VGAM1768 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1768 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1768 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59170] VGAM1768 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1768 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1768 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1768 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1768 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59171] The complementary binding of VGAM1768 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1768 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1768 host target RNA into VGAM1768 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59172] It is appreciated that VGAM1768 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1768 host target genes. The mRNA of each one of this plurality of VGAM1768 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1768 RNA, herein designated VGAM RNA, and which when bound by VGAM1768 RNA causes inhibition of translation of respective one or more VGAM1768 host target proteins.

[59173] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1768 gene, herein designated VGAM GENE, on one or more VGAM1768 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59174] It is yet further appreciated that a function of VGAM1768 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1768 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM1768 correlate with, and may be deduced from, the identity of the host target genes which VGAM1768 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59175] Nucleotide sequences of the VGAM1768 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1768 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1768 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1768 are further described hereinbelow with reference to Table 1.

[59176] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1768 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1768 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[59177] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1768 gene, herein designated VGAM is inhibition of expression of VGAM1768 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1768 correlate with, and may be deduced from, the identity of the target genes which VGAM1768 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59178] LOC93538 (Accession XM\_051927) is a VGAM1768 host target gene. LOC93538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93538 BINDING SITE, designated SEQ ID:35921, to the nucleotide sequence of VGAM1768 RNA, herein designated VGAM RNA, also designated SEQ ID:4479.

[59179] A function of VGAM1768 is therefore inhibition of LOC93538 (Accession XM\_051927). Accordingly, utilities of VGAM1768 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC93538. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1769 (VGAM1769) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59180] VGAM1769 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1769 was detected is described hereinabove with reference to Figs. 1–8.

[59181] VGAM1769 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM1769 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59182] VGAM1769 gene encodes a VGAM1769 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1769 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1769 precursor RNA is designated SEQ ID:1755, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1755 is located at position 123 relative to the genome of Rabbit Fibroma Virus.

- [59183] VGAM1769 precursor RNA folds onto itself, forming VGAM1769 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [59184] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1769 folded precursor RNA into VGAM1769 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1769 RNA is designated SEQ ID:4480, and is provided hereinbelow with reference to the sequence listing part.



[59185] VGAM1769 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1769 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1769 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59186] VGAM1769 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1769 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1769 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1769 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1769 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[59187] The complementary binding of VGAM1769 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1769 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1769 host target RNA into VGAM1769 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59188] It is appreciated that VGAM1769 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1769 host target genes. The mRNA of each one of this plurality of VGAM1769 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1769 RNA, herein designated VGAM RNA, and which when bound by VGAM1769 RNA causes

inhibition of translation of respective one or more VGAM1769 host target proteins.

[59189] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1769 gene, herein designated VGAM GENE, on one or more VGAM1769 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59190] It is yet further appreciated that a function of VGAM1769 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1769 include diagnosis, prevention and

treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM1769 correlate with, and may be deduced from, the identity of the host target genes which VGAM1769 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59191] Nucleotide sequences of the VGAM1769 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1769 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1769 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1769 are further described hereinbelow with reference to Table 1.

[59192] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1769 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1769 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59193] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1769 gene, herein designated VGAM is inhibition of expression of VGAM1769 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1769 correlate with, and may be deduced from, the identity of the target genes which VGAM1769 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59194] Collagen, Type IV, Alpha 5 (Alport syndrome) (COL4A5, Accession NM\_000495) is a VGAM1769 host target gene. COL4A5 BINDING SITE1 through COL4A5 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL4A5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A5 BINDING SITE1 through COL4A5 BINDING SITE3, designated SEQ ID:6110, SEQ ID:27213 and SEQ ID:27216 respectively, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59195] A function of VGAM1769 is therefore inhibition of Collagen, Type IV, Alpha 5 (Alport syndrome) (COL4A5, Accession NM\_000495). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A5. SIP (Accession

NM\_014412) is another VGAM1769 host target gene. SIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIP BINDING SITE, designated SEQ ID:15758, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59196] Another function of VGAM1769 is therefore inhibition of SIP (Accession NM\_014412). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIP. Cadherin-like 26 (CDH26, Accession NM\_021810) is another VGAM1769 host target gene. CDH26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH26 BINDING SITE, designated SEQ ID:22372, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59197] Another function of VGAM1769 is therefore inhibition of Cadherin-like 26 (CDH26, Accession NM\_021810). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH26. FLJ12604 (Accession XM\_035022) is another VGAM1769 host target gene. FLJ12604 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12604, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12604 BINDING SITE, designated SEQ ID:32193, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59198] Another function of VGAM1769 is therefore inhibition of FLJ12604 (Accession XM\_035022). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12604. Hypermethylated In Cancer 2 (HIC2, Accession XM\_036937) is another VGAM1769 host target gene. HIC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIC2, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC2 BINDING SITE, designated SEQ ID:32534, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59199] Another function of VGAM1769 is therefore inhibition of Hypermethylated In Cancer 2 (HIC2, Accession XM\_036937). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC2. KIAA1255 (Accession XM\_040626) is another VGAM1769 host target gene. KIAA1255 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1255, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1255 BINDING SITE, designated SEQ ID:33348, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59200] Another function of VGAM1769 is therefore inhibition of KIAA1255 (Accession XM\_040626). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with KIAA1255. MGC11257 (Accession NM\_032350) is another VGAM1769 host target gene. MGC11257 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11257 BINDING SITE, designated SEQ ID:26140, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59201] Another function of VGAM1769 is therefore inhibition of MGC11257 (Accession NM\_032350). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11257. Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM\_015550) is another VGAM1769 host target gene. OSBPL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL3 BINDING SITE, designated SEQ

ID:17818, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59202] Another function of VGAM1769 is therefore inhibition of Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM\_015550). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL3. LOC113763 (Accession NM\_138434) is another VGAM1769 host target gene. LOC113763 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC113763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113763 BINDING SITE, designated SEQ ID:28806, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59203] Another function of VGAM1769 is therefore inhibition of LOC113763 (Accession NM\_138434). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113763. LOC130595 (Accession XM\_065793) is an-

other VGAM1769 host target gene. LOC130595 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC130595, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130595 BINDING SITE, designated SEQ ID:37300, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59204] Another function of VGAM1769 is therefore inhibition of LOC130595 (Accession XM\_065793). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130595. LOC199796 (Accession XM\_058994) is another VGAM1769 host target gene. LOC199796 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199796 BINDING SITE, designated SEQ ID:36809, to the nucleotide sequence of VGAM1769 RNA, herein designated VGAM RNA, also designated SEQ ID:4480.

[59205] Another function of VGAM1769 is therefore inhibition of LOC199796 (Accession XM\_058994). Accordingly, utilities of VGAM1769 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199796. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1770 (VGAM1770) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59206] VGAM1770 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1770 was detected is described hereinabove with reference to Figs. 1–8.

[59207] VGAM1770 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM1770 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59208] VGAM1770 gene encodes a VGAM1770 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1770 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1770 precursor RNA is designated SEQ ID:1756, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1756 is located at position 8292 relative to the genome of Rabbit Fibroma Virus.

- [59209] VGAM1770 precursor RNA folds onto itself, forming VGAM1770 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [59210] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1770 folded precursor RNA into VGAM1770 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1770 RNA is designated SEQ ID:4481, and is provided hereinbelow with reference to the sequence listing part.

[59211] VGAM1770 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1770 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1770 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59212] VGAM1770 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1770 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1770 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1770 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1770 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59213] The complementary binding of VGAM1770 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1770 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1770 host target RNA into VGAM1770 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59214] It is appreciated that VGAM1770 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1770 host target genes. The mRNA of each one of this plurality of VGAM1770 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1770 RNA, herein designated VGAM RNA, and which when bound by VGAM1770 RNA causes inhibition of translation of respective one or more VGAM1770 host target proteins.

[59215] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1770 gene, herein designated VGAM GENE, on one or more VGAM1770 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).



[59216] It is yet further appreciated that a function of VGAM1770 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM1770 correlate with, and may be deduced from, the identity of the host target genes which VGAM1770 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59217] Nucleotide sequences of the VGAM1770 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1770 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1770 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1770 are further described hereinbelow with reference to Table 1.

[59218] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1770 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1770 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[59219] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1770 gene, herein designated VGAM is inhibition of expression of VGAM1770 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1770 correlate with, and may be deduced from, the identity of the target genes which VGAM1770 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59220] Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession NM\_138271) is a VGAM1770 host target gene. ATRX BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ATRX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATRX BINDING SITE, designated SEQ ID:28682, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59221] A function of VGAM1770 is therefore inhibition of Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession

NM\_138271). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATRX. Chromosome 1 Open Reading Frame 6 (C1orf6, Accession NM\_020131) is another VGAM1770 host target gene. C1orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf6 BINDING SITE, designated SEQ ID:21330, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59222] Another function of VGAM1770 is therefore inhibition of Chromosome 1 Open Reading Frame 6 (C1orf6, Accession NM\_020131), a gene which may link ataxin-1 with the chaperone and ubiquitin/proteasome pathways. Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf6. The function of C1orf6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1286. Fibulin 1 (FBLN1,

Accession NM\_006485) is another VGAM1770 host target gene. FBLN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBLN1 BINDING SITE, designated SEQ ID:13213, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59223] Another function of VGAM1770 is therefore inhibition of Fibulin 1 (FBLN1, Accession NM\_006485), a gene which secreted glycoprotein; has EGF-like repeats, similar to anaphylatoxins C3a, C4a, and C5a. Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBLN1. The function of FBLN1 has been established by previous studies. Fibulin-1 was first described as an integrin-binding fibulin from human placenta by Argraves et al. (1989), who found that it is a secreted glycoprotein that becomes incorporated into a fibrillar extracellular matrix when expressed in cultured cells or added exogenously to cell monolayers. Preliminary electron micro-

scopic data suggested a rod-like structure for fibulin-1, consistent with the sequence predictions. Calcium-binding to fibulin-1 is apparently required to mediate its binding to laminin and nidogen (OMIM Ref. No. 131390). By in situ hybridization of tritium-labeled cDNA probes, Mattei et al. (1994) assigned the human FBLN1 gene to 22q13.2-q13.3 and assigned its counterpart in mouse to the E-F band of chromosome 15. Korenberg et al. (1995) assigned the FBLN1 gene to 22q13.3 by fluorescence in situ hybridization.

[59224] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59225] Korenberg, J. R.; Chen, X.-N.; Tran, H.; Argraves, W. S. : Localization of the human gene for fibulin-1 (FBLN1) to chromosome band 22q13.3. *Cytogenet. Cell Genet.* 68: 192-193, 1995. ; and

[59226] Mattei, M.-G.; Pan, T.-C.; Zhang, R.-Z.; Timpl, R.; Chu, M.-L. : The fibulin-1 gene (FBLN1) is located on human chromosome 22 and on mouse chromosome 15. *Genomics* 22: 437-438, 1994.

[59227] Further studies establishing the function and utilities of FBLN1 are found in John Hopkins OMIM database record

ID 135820, and in cited publications numbered 3464–3466 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 6 (KCNA6, Accession NM\_002235) is another VGAM1770 host target gene. KCNA6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNA6 BINDING SITE, designated SEQ ID:8020, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59228] Another function of VGAM1770 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 6 (KCNA6, Accession NM\_002235), a gene which mediates the voltage-dependent potassium ion permeability of excitable membranes. Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNA6. The function of KCNA6 and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM893. Sodium Channel, Nonvoltage-gated 1, Gamma (SCNN1G, Accession NM\_001039) is another VGAM1770 host target gene. SCNN1G BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCNN1G, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCNN1G BINDING SITE, designated SEQ ID:6705, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59229] Another function of VGAM1770 is therefore inhibition of Sodium Channel, Nonvoltage-gated 1, Gamma (SCNN1G, Accession NM\_001039). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCNN1G. Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM\_024331) is another VGAM1770 host target gene. C20orf121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf121 BINDING SITE, designated SEQ ID:23637, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59230] Another function of VGAM1770 is therefore inhibition of Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM\_024331). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf121. FK506 Binding Protein 9, 63 KDa (FKBP9, Accession XM\_168403) is another VGAM1770 host target gene. FKBP9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FKBP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKBP9 BINDING SITE, designated SEQ ID:45143, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59231] Another function of VGAM1770 is therefore inhibition of FK506 Binding Protein 9, 63 KDa (FKBP9, Accession



XM\_168403). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKBP9. FLJ10661 (Accession NM\_018172) is another VGAM1770 host target gene.

FLJ10661 BINDING SITE1 and FLJ10661 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10661, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10661 BINDING SITE1 and FLJ10661 BINDING SITE2, designated SEQ ID:19998 and SEQ ID:19999 respectively, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59232] Another function of VGAM1770 is therefore inhibition of FLJ10661 (Accession NM\_018172). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10661. ICK (Accession NM\_016513) is another VGAM1770 host target gene. ICK BINDING SITE1 and ICK BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ICK, corresponding to HOST TARGET binding sites such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICK BINDING SITE1 and ICK BINDING SITE2, designated SEQ ID:18593 and SEQ ID:17193 respectively, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59233] Another function of VGAM1770 is therefore inhibition of ICK (Accession NM\_016513). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICK. KIAA0892 (Accession XM\_048457) is another VGAM1770 host target gene. KIAA0892 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0892, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0892 BINDING SITE, designated SEQ ID:35173, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59234] Another function of VGAM1770 is therefore inhibition of KIAA0892 (Accession XM\_048457). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0892. Lipoma HMGIC Fusion Partner (LHFP, Accession NM\_005780) is another VGAM1770 host target gene. LHFP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LHFP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LHFP BINDING SITE, designated SEQ ID:12357, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59235] Another function of VGAM1770 is therefore inhibition of Lipoma HMGIC Fusion Partner (LHFP, Accession NM\_005780). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LHFP. MAC30 (Accession XM\_031536) is another VGAM1770 host target gene. MAC30 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MAC30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAC30 BINDING SITE, designated SEQ

ID:31401, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59236] Another function of VGAM1770 is therefore inhibition of MAC30 (Accession XM\_031536). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAC30. Purinergic Receptor P2X, Ligand-gated Ion Channel, 5 (P2RX5, Accession NM\_002561) is another VGAM1770 host target gene. P2RX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P2RX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RX5 BINDING SITE, designated SEQ ID:8409, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59237] Another function of VGAM1770 is therefore inhibition of Purinergic Receptor P2X, Ligand-gated Ion Channel, 5 (P2RX5, Accession NM\_002561). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RX5.

LOC149577 (Accession XM\_097675) is another VGAM1770 host target gene. LOC149577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149577 BINDING SITE, designated SEQ ID:41026, to the nucleotide sequence of VGAM1770 RNA, herein designated VGAM RNA, also designated SEQ ID:4481.

[59238] Another function of VGAM1770 is therefore inhibition of LOC149577 (Accession XM\_097675). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149577. LOC153196 (Accession XM\_098323) is another VGAM1770 host target gene. LOC153196 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153196 BINDING SITE, designated SEQ ID:41594, to the nucleotide sequence of VGAM1770 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4481.

[59239] Another function of VGAM1770 is therefore inhibition of LOC153196 (Accession XM\_098323). Accordingly, utilities of VGAM1770 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153196. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1771 (VGAM1771) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59240] VGAM1771 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1771 was detected is described hereinabove with reference to Figs. 1–8.

[59241] VGAM1771 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pestivirus Type 1. VGAM1771 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59242] VGAM1771 gene encodes a VGAM1771 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1771 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1771 precursor RNA is designated SEQ ID:1757, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1757 is located at position 3477 relative to the genome of Pestivirus Type 1.

[59243] VGAM1771 precursor RNA folds onto itself, forming VGAM1771 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59244] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1771 folded precursor RNA into VGAM1771 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1771 RNA is designated SEQ ID:4482, and is provided hereinbelow with reference to the sequence listing part.

[59245] VGAM1771 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1771 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1771 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59246] VGAM1771 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1771 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1771 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and



BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1771 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1771 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[59247] The complementary binding of VGAM1771 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1771 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1771 host target RNA into VGAM1771 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59248] It is appreciated that VGAM1771 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1771 host target genes. The mRNA of

each one of this plurality of VGAM1771 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1771 RNA, herein designated VGAM RNA, and which when bound by VGAM1771 RNA causes inhibition of translation of respective one or more VGAM1771 host target proteins.

[59249] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1771 gene, herein designated VGAM GENE, on one or more VGAM1771 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[59250] It is yet further appreciated that a function of VGAM1771 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of viral infection by Pestivirus Type 1. Specific functions, and accordingly utilities, of VGAM1771 correlate with, and may be deduced from, the identity of the host target genes which VGAM1771 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59251] Nucleotide sequences of the VGAM1771 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1771 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1771 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1771 are further described hereinbelow with reference to Table 1.

[59252] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1771 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1771 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59253] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1771 gene, herein designated VGAM is inhibition of expression of VGAM1771 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1771 correlate with, and may be deduced from, the identity of the target genes which VGAM1771 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59254] Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession NM\_000134) is a VGAM1771 host target gene. FABP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FABP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FABP2 BINDING SITE, designated SEQ ID:5622, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59255] A function of VGAM1771 is therefore inhibition of Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession NM\_000134), a gene which may have a role in dietary fat

uptake or processing. Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FABP2. The function of FABP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM951. Leucine Zipper Protein 1 (LUZP1, Accession NM\_033631) is another VGAM1771 host target gene. LUZP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LUZP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LUZP1 BINDING SITE, designated SEQ ID:27354, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59256] Another function of VGAM1771 is therefore inhibition of Leucine Zipper Protein 1 (LUZP1, Accession NM\_033631). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LUZP1. Sine Oculis Homeobox Homolog 2 (Drosophila) (SIX2, Accession NM\_016932) is an-

other VGAM1771 host target gene. SIX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIX2 BINDING SITE, designated SEQ ID:18849, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59257] Another function of VGAM1771 is therefore inhibition of Sine Oculis Homeobox Homolog 2 (Drosophila) (SIX2, Accession NM\_016932), a gene which may be involved in limb tendon and ligament development (by similarity). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIX2. The function of SIX2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1151. Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 1 (STAM, Accession NM\_003473) is another VGAM1771 host target gene. STAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

STAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAM BINDING SITE, designated SEQ ID:9541, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59258] Another function of VGAM1771 is therefore inhibition of Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 1 (STAM, Accession NM\_003473), a gene which is as an adaptor molecule involved in the downstream signaling of cytokine receptors. Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAM. The function of STAM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM927.FLJ10724 (Accession NM\_018194) is another VGAM1771 host target gene. FLJ10724 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10724, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FLJ10724 BINDING SITE, designated SEQ ID:20053, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59259] Another function of VGAM1771 is therefore inhibition of FLJ10724 (Accession NM\_018194). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10724. FLJ13072 (Accession XM\_117117) is another VGAM1771 host target gene. FLJ13072 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13072 BINDING SITE, designated SEQ ID:43232, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59260] Another function of VGAM1771 is therefore inhibition of FLJ13072 (Accession XM\_117117). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13072. GENX-3414 (Accession NM\_003943) is another VGAM1771 host target gene. GENX-3414 BINDING SITE is



HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GENX-3414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GENX-3414 BINDING SITE, designated SEQ ID:10058, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59261] Another function of VGAM1771 is therefore inhibition of GENX-3414 (Accession NM\_003943). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GENX-3414. KIAA0430 (Accession NM\_019081) is another VGAM1771 host target gene. KIAA0430 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0430 BINDING SITE, designated SEQ ID:21150, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59262] Another function of VGAM1771 is therefore inhibition of

KIAA0430 (Accession NM\_019081). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0430. KIAA0992 (Accession NM\_016081) is another VGAM1771 host target gene. KIAA0992 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0992 BINDING SITE, designated SEQ ID:18157, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59263] Another function of VGAM1771 is therefore inhibition of KIAA0992 (Accession NM\_016081). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0992. KIAA1466 (Accession XM\_050285) is another VGAM1771 host target gene. KIAA1466 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1466 BINDING SITE, designated SEQ ID:35601, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59264] Another function of VGAM1771 is therefore inhibition of KIAA1466 (Accession XM\_050285). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1466. KIAA1500 (Accession XM\_034353) is another VGAM1771 host target gene. KIAA1500 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1500, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1500 BINDING SITE, designated SEQ ID:32069, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59265] Another function of VGAM1771 is therefore inhibition of KIAA1500 (Accession XM\_034353). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1500. KIAA1613 (Accession XM\_035946) is another

VGAM1771 host target gene. KIAA1613 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1613, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1613 BINDING SITE, designated SEQ ID:32360, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59266] Another function of VGAM1771 is therefore inhibition of KIAA1613 (Accession XM\_035946). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1613. KIAA1977 (Accession XM\_058800) is another VGAM1771 host target gene. KIAA1977 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1977 BINDING SITE, designated SEQ ID:36747, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59267] Another function of VGAM1771 is therefore inhibition of KIAA1977 (Accession XM\_058800). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1977. LAK-4P (Accession NM\_007267) is another VGAM1771 host target gene. LAK-4P BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LAK-4P, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAK-4P BINDING SITE, designated SEQ ID:14131, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59268] Another function of VGAM1771 is therefore inhibition of LAK-4P (Accession NM\_007267). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAK-4P. MGC35558 (Accession NM\_145013) is another VGAM1771 host target gene. MGC35558 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC35558, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC35558 BINDING SITE, designated SEQ ID:29612, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59269] Another function of VGAM1771 is therefore inhibition of MGC35558 (Accession NM\_145013). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC35558. Makorin, Ring Finger Protein, 1 (MKRN1, Accession NM\_013446) is another VGAM1771 host target gene. MKRN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MKRN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKRN1 BINDING SITE, designated SEQ ID:15112, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59270] Another function of VGAM1771 is therefore inhibition of Makorin, Ring Finger Protein, 1 (MKRN1, Accession NM\_013446). Accordingly, utilities of VGAM1771 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with MKRN1. Protein Kinase C and Casein Kinase Substrate In Neurons 2 (PACSIN2, Accession NM\_007229) is another VGAM1771 host target gene. PACSIN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACSIN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACSIN2 BINDING SITE, designated SEQ ID:14095, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59271] Another function of VGAM1771 is therefore inhibition of Protein Kinase C and Casein Kinase Substrate In Neurons 2 (PACSIN2, Accession NM\_007229). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACSIN2. RRP4 (Accession NM\_014285) is another VGAM1771 host target gene. RRP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RRP4 BINDING SITE, designated SEQ ID:15560, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59272] Another function of VGAM1771 is therefore inhibition of RRP4 (Accession NM\_014285). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RRP4. SIMRP7 (Accession XM\_166462) is another VGAM1771 host target gene. SIMRP7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIMRP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIMRP7 BINDING SITE, designated SEQ ID:44368, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59273] Another function of VGAM1771 is therefore inhibition of SIMRP7 (Accession XM\_166462). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIMRP7.



LOC145783 (Accession XM\_085231) is another VGAM1771 host target gene. LOC145783 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145783, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145783 BINDING SITE, designated SEQ ID:37976, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59274] Another function of VGAM1771 is therefore inhibition of LOC145783 (Accession XM\_085231). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145783. LOC220514 (Accession XM\_017498) is another VGAM1771 host target gene. LOC220514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220514 BINDING SITE, designated SEQ ID:30320, to the nucleotide sequence of VGAM1771 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4482.

[59275] Another function of VGAM1771 is therefore inhibition of LOC220514 (Accession XM\_017498). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220514. LOC220930 (Accession XM\_167624) is another VGAM1771 host target gene. LOC220930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220930 BINDING SITE, designated SEQ ID:44732, to the nucleotide sequence of VGAM1771 RNA, herein designated VGAM RNA, also designated SEQ ID:4482.

[59276] Another function of VGAM1771 is therefore inhibition of LOC220930 (Accession XM\_167624). Accordingly, utilities of VGAM1771 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220930. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1772 (VGAM1772) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59277] VGAM1772 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1772 was detected is described hereinabove with reference to Figs. 1–8.

[59278] VGAM1772 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pestivirus Type 1. VGAM1772 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59279] VGAM1772 gene encodes a VGAM1772 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1772 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1772 precursor RNA is designated SEQ ID:1758, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1758 is located at position 2037 relative to the genome of Pestivirus Type 1.

[59280] VGAM1772 precursor RNA folds onto itself, forming

VGAM1772 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59281] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1772 folded precursor RNA into VGAM1772 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1772 RNA is designated SEQ ID:4483, and is provided hereinbelow with reference to the sequence listing part.

[59282] VGAM1772 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1772 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1772 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59283] VGAM1772 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1772 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1772 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1772 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1772 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59284] The complementary binding of VGAM1772 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1772 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1772 host target RNA into VGAM1772 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59285] It is appreciated that VGAM1772 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1772 host target genes. The mRNA of each one of this plurality of VGAM1772 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1772 RNA, herein designated VGAM RNA, and which when bound by VGAM1772 RNA causes inhibition of translation of respective one or more VGAM1772 host target proteins.

[59286] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1772 gene, herein designated VGAM GENE, on one or more VGAM1772 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59287] It is yet further appreciated that a function of VGAM1772 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1772 include diagnosis, prevention and treatment of viral infection by Pestivirus Type 1. Specific functions, and accordingly utilities, of VGAM1772 correlate with, and may be deduced from, the identity of the host target genes which VGAM1772 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[59288] Nucleotide sequences of the VGAM1772 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1772 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1772 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1772 are further described hereinbelow with reference to Table 1.

[59289] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1772 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1772 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59290] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1772 gene, herein designated VGAM is inhibition of expression of VGAM1772 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1772 correlate with, and may be deduced from, the identity of the target genes which VGAM1772 binds and inhibits, and the function of these target genes,



as elaborated hereinbelow.

[59291] MHC Class II Transactivator (MHC2TA, Accession NM\_000246) is a VGAM1772 host target gene. MHC2TA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MHC2TA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MHC2TA BINDING SITE, designated SEQ ID:5775, to the nucleotide sequence of VGAM1772 RNA, herein designated VGAM RNA, also designated SEQ ID:4483.

[59292] A function of VGAM1772 is therefore inhibition of MHC Class II Transactivator (MHC2TA, Accession NM\_000246). Accordingly, utilities of VGAM1772 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MHC2TA. Rho Guanine Nucleotide Exchange Factor (GEF) 3 (ARHGEF3, Accession NM\_019555) is another VGAM1772 host target gene. ARHGEF3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARHGEF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF3 BINDING SITE, designated SEQ ID:21208, to the nucleotide sequence of VGAM1772 RNA, herein designated VGAM RNA, also designated SEQ ID:4483.

[59293] Another function of VGAM1772 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 3 (ARHGEF3, Accession NM\_019555). Accordingly, utilities of VGAM1772 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF3. Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM\_006379) is another VGAM1772 host target gene. SEMA3C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA3C BINDING SITE, designated SEQ ID:13071, to the nucleotide sequence of VGAM1772 RNA, herein designated VGAM RNA, also designated SEQ ID:4483.

[59294] Another function of VGAM1772 is therefore inhibition of

Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM\_006379). Accordingly, utilities of VGAM1772 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA3C. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1773 (VGAM1773) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59295] VGAM1773 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1773 was detected is described hereinabove with reference to Figs. 1–8.

[59296] VGAM1773 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1773 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59297] VGAM1773 gene encodes a VGAM1773 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1773 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1773 precursor RNA is designated SEQ ID:1759, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1759 is located at position 6368 relative to the genome of Cryphonectria Hypovirus 1.

[59298] VGAM1773 precursor RNA folds onto itself, forming VGAM1773 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59299] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1773 folded precursor RNA into VGAM1773 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1773 RNA is designated SEQ ID:4484, and is provided hereinbelow with reference to the sequence listing part.

[59300] VGAM1773 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1773 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1773 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[59301] VGAM1773 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1773 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1773 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1773 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1773 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59302] The complementary binding of VGAM1773 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1773 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1773 host target RNA into VGAM1773 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59303] It is appreciated that VGAM1773 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1773 host target genes. The mRNA of each one of this plurality of VGAM1773 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1773 RNA, herein designated VGAM RNA, and which when bound by VGAM1773 RNA causes inhibition of translation of respective one or more VGAM1773 host target proteins.

[59304] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1773 gene, herein designated VGAM GENE, on one or more VGAM1773 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59305] It is yet further appreciated that a function of VGAM1773 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1773 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGAM1773 correlate with, and may be deduced from, the identity of the host target genes which VGAM1773 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59306] Nucleotide sequences of the VGAM1773 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1773 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1773 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1773 are further described hereinbelow with reference to Table 1.

[59307] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1773 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1773 RNA, herein designated VGAM RNA, are described hereinbelow



with reference to Table 2.

[59308] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1773 gene, herein designated VGAM is inhibition of expression of VGAM1773 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1773 correlate with, and may be deduced from, the identity of the target genes which VGAM1773 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59309] Paired Box Gene 4 (PAX4, Accession NM\_006193) is a VGAM1773 host target gene. PAX4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAX4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAX4 BINDING SITE, designated SEQ ID:12865, to the nucleotide sequence of VGAM1773 RNA, herein designated VGAM RNA, also designated SEQ ID:4484.

[59310] A function of VGAM1773 is therefore inhibition of Paired Box Gene 4 (PAX4, Accession NM\_006193), a gene which involves in the differentiation of endoderm-derived endocrine pancreas. Accordingly, utilities of VGAM1773 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with PAX4. The function of PAX4 has been established by previous studies. Bonthron et al. (1998) described the partial structure of PAX4, including the entire coding region. They found that the gene has 10 exons, with the paired domain and homeodomain contained in 6 exons, which they named B to G. By searching sequence databases with a mouse Pax4 cDNA, Matsushita et al. (1998) and Inoue et al. (1998) identified a human cosmid clone that maps to chromosome 7q31.3 and contains the human PAX4 sequence. The human PAX4 gene encodes a deduced 350-amino acid protein that is 80% identical to the deduced mouse Pax4 protein. RT-PCR detected mouse Pax4 expression in pancreatic islets and islet beta cell lines, but not in the other 13 adult mouse organs examined (Matsushita et al., 1998). Pilz et al. (1993) used mouse Pax4 cDNAs as probes to map the human homolog to chromosome 7 in somatic cell hybrids. By use of hybrids carrying translocated chromosomes, they showed that the human PAX4 gene is located on 7q22-qter. Animal model experiments lend further support to the function of PAX4. Sosa-Pineda et al. (1997) showed by study of knockout mice that the Pax4 gene is

essential for differentiation of insulin-producing beta-cells in mammalian pancreas. See also PAX6 (OMIM Ref. No. 607108) and St-Onge et al. (1997), who concluded that both PAX4 and PAX6 genes are required for endocrine fate in the pancreas.

[59311] It is appreciated that the abovementioned animal model for PAX4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[59312] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59313] Matsushita, T.; Yamaoka, T.; Otsuka, S.; Moritani, M.; Matsumoto, T.; Itakura, M. : Molecular cloning of mouse paired-box-containing gene (Pax)-4 from an islet beta cell line and deduced sequence of human Pax-4. Biochem. Biophys. Res. Commun. 242: 176-180, 1998. ; and

[59314] Sosa-Pineda, B.; Chowdhury, K.; Torres, M.; Oliver, G.; Gruss, P. : The Pax4 gene is essential for differentiation of insulin-producing beta cells in the mammalian pancreas. Nature 386:.

[59315] Further studies establishing the function and utilities of PAX4 are found in John Hopkins OMIM database record ID

167413, and in cited publications numbered 10758–10761, 10338, 10762–10763, 1071 and 10764 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATP-binding Cassette, Sub-family A (ABC1), Member 5 (ABCA5, Accession NM\_018672) is another VGAM1773 host target gene. ABCA5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ABCA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCA5 BINDING SITE, designated SEQ ID:20746, to the nucleotide sequence of VGAM1773 RNA, herein designated VGAM RNA, also designated SEQ ID:4484.

[59316] Another function of VGAM1773 is therefore inhibition of ATP-binding Cassette, Sub-family A (ABC1), Member 5 (ABCA5, Accession NM\_018672). Accordingly, utilities of VGAM1773 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCA5. Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 12 (PSMD12, Accession NM\_002816) is another VGAM1773 host target gene. PSMD12 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMD12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMD12 BINDING SITE, designated SEQ ID:8680, to the nucleotide sequence of VGAM1773 RNA, herein designated VGAM RNA, also designated SEQ ID:4484.

[59317] Another function of VGAM1773 is therefore inhibition of Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 12 (PSMD12, Accession NM\_002816). Accordingly, utilities of VGAM1773 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMD12. TAF2 RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 150kDa (TAF2, Accession NM\_003184) is another VGAM1773 host target gene. TAF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF2 BINDING SITE, designated SEQ ID:9161, to the nucleotide sequence of VGAM1773 RNA, herein

designated VGAM RNA, also designated SEQ ID:4484.

[59318] Another function of VGAM1773 is therefore inhibition of TAF2 RNA Polymerase II, TATA Box Binding Protein (TBP)–associated Factor, 150kDa (TAF2, Accession NM\_003184). Accordingly, utilities of VGAM1773 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1774 (VGAM1774) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59319] VGAM1774 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1774 was detected is described hereinabove with reference to Figs. 1–8.

[59320] VGAM1774 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1774 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59321] VGAM1774 gene encodes a VGAM1774 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1774 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1774 precursor RNA is designated SEQ ID:1760, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1760 is located at position 10666 relative to the genome of Cryphonectria Hypovirus 1.

[59322] VGAM1774 precursor RNA folds onto itself, forming VGAM1774 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59323] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1774 folded precursor RNA into VGAM1774 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1774 RNA is designated SEQ ID:4485, and is provided hereinbelow with reference to the sequence listing part.

[59324] VGAM1774 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1774 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1774 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59325] VGAM1774 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1774 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1774 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding



sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1774 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1774 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59326] The complementary binding of VGAM1774 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1774 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1774 host target RNA into VGAM1774 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59327] It is appreciated that VGAM1774 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1774 host target genes. The mRNA of each one of this plurality of VGAM1774 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1774 RNA, herein designated VGAM RNA, and which when bound by VGAM1774 RNA causes inhibition of translation of respective one or more VGAM1774 host target proteins.

[59328] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1774 gene, herein designated VGAM GENE, on one or more VGAM1774 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[59329] It is yet further appreciated that a function of VGAM1774 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGAM1774 correlate with, and may be deduced from, the identity of the host target genes which VGAM1774 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59330] Nucleotide sequences of the VGAM1774 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1774 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1774 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1774 are further described hereinbelow with reference to Table 1.

[59331] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1774 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1774 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59332] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1774 gene, herein designated VGAM is inhibition of expression of VGAM1774 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1774 correlate with, and may be deduced from, the identity of the target genes which VGAM1774 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59333] Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 3 (MLLT3, Accession NM\_004529) is a VGAM1774 host target gene. MLLT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLLT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT3 BINDING SITE, designated SEQ ID:10867, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59334] A function of VGAM1774 is therefore inhibition of

Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 3 (MLLT3, Accession NM\_004529), a gene which is Serine and proline rich protein. Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT3. The function of MLLT3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM67. Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, Drosophila) (PDE4D, Accession XM\_056815) is another VGAM1774 host target gene. PDE4D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4D BINDING SITE, designated SEQ ID:36425, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59335] Another function of VGAM1774 is therefore inhibition of Phosphodiesterase 4D, CAMP-specific (phosphodiesterase

E3 dunce homolog, Drosophila) (PDE4D, Accession XM\_056815), a gene which has similarity to Drosophila dnc, which is the affected protein in learning and memory mutant dunce. Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4D. The function of PDE4D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Parathyroid Hormone-like Hormone (PTH LH, Accession NM\_002820) is another VGAM1774 host target gene. PTH LH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTH LH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTH LH BINDING SITE, designated SEQ ID:8685, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59336] Another function of VGAM1774 is therefore inhibition of Parathyroid Hormone-like Hormone (PTH LH, Accession NM\_002820), a gene which plays a physiological role in

lactation, possibly as a hormone for the mobilization and/or transfer of calcium to the milk. Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTHLH. The function of PTHLH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1590. Rho Guanine Nucleotide Exchange Factor (GEF) 3 (ARHGEF3, Accession NM\_019555) is another VGAM1774 host target gene. ARHGEF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF3 BINDING SITE, designated SEQ ID:21210, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59337] Another function of VGAM1774 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 3 (ARHGEF3, Accession NM\_019555). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

ARHGEF3. DKFZP434I0714 (Accession XM\_098247) is another VGAM1774 host target gene. DKFZP434I0714 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434I0714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I0714 BINDING SITE, designated SEQ ID:41528, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59338] Another function of VGAM1774 is therefore inhibition of DKFZP434I0714 (Accession XM\_098247). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I0714. DKFZP586F1524 (Accession NM\_015584) is another VGAM1774 host target gene. DKFZP586F1524 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586F1524, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586F1524 BINDING SITE,



designated SEQ ID:17851, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59339] Another function of VGAM1774 is therefore inhibition of DKFZP586F1524 (Accession NM\_015584). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586F1524. FLJ10815 (Accession NM\_018231) is another VGAM1774 host target gene. FLJ10815 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10815, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10815 BINDING SITE, designated SEQ ID:20173, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59340] Another function of VGAM1774 is therefore inhibition of FLJ10815 (Accession NM\_018231). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10815. FLJ22415 (Accession XM\_166168) is another VGAM1774 host target gene. FLJ22415 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22415 BINDING SITE, designated SEQ ID:43983, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59341] Another function of VGAM1774 is therefore inhibition of FLJ22415 (Accession XM\_166168). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22415. KIAA0820 (Accession XM\_044463) is another VGAM1774 host target gene. KIAA0820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0820 BINDING SITE, designated SEQ ID:34214, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59342] Another function of VGAM1774 is therefore inhibition of

KIAA0820 (Accession XM\_044463). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0820. KIAA1863 (Accession XM\_036104) is another VGAM1774 host target gene. KIAA1863 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1863, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1863 BINDING SITE, designated SEQ ID:32379, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59343] Another function of VGAM1774 is therefore inhibition of KIAA1863 (Accession XM\_036104). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1863. LIG-1 (Accession XM\_033712) is another VGAM1774 host target gene. LIG-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIG-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LIG-1 BINDING SITE, designated SEQ ID:31952, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59344] Another function of VGAM1774 is therefore inhibition of LIG-1 (Accession XM\_033712). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIG-1. NCE2 (Accession NM\_080678) is another VGAM1774 host target gene. NCE2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCE2 BINDING SITE, designated SEQ ID:27971, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59345] Another function of VGAM1774 is therefore inhibition of NCE2 (Accession NM\_080678). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCE2. Protocadherin 19 (PCDH19, Accession XM\_033173) is an-

other VGAM1774 host target gene. PCDH19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH19 BINDING SITE, designated SEQ ID:31857, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59346] Another function of VGAM1774 is therefore inhibition of Protocadherin 19 (PCDH19, Accession XM\_033173). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH19. RNAC (Accession NM\_005772) is another VGAM1774 host target gene. RNAC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNAC BINDING SITE, designated SEQ ID:12343, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59347] Another function of VGAM1774 is therefore inhibition of RNAC (Accession NM\_005772). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNAC. STRIN (Accession NM\_016271) is another VGAM1774 host target gene. STRIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STRIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRIN BINDING SITE, designated SEQ ID:18394, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59348] Another function of VGAM1774 is therefore inhibition of STRIN (Accession NM\_016271). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRIN. Three Prime Repair Exonuclease 1 (TREX1, Accession NM\_033628) is another VGAM1774 host target gene. TREX1 BINDING SITE1 and TREX1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TREX1, corresponding to HOST TARGET

binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TREX1 BINDING SITE1 and TREX1 BINDING SITE2, designated SEQ ID:27343 and SEQ ID:27334 respectively, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59349] Another function of VGAM1774 is therefore inhibition of Three Prime Repair Exonuclease 1 (TREX1, Accession NM\_033628). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TREX1. LOC124602 (Accession XM\_058829) is another VGAM1774 host target gene. LOC124602 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC124602, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124602 BINDING SITE, designated SEQ ID:36755, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59350] Another function of VGAM1774 is therefore inhibition of

LOC124602 (Accession XM\_058829). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124602. LOC163397 (Accession XM\_099133) is another VGAM1774 host target gene. LOC163397 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163397 BINDING SITE, designated SEQ ID:42081, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59351] Another function of VGAM1774 is therefore inhibition of LOC163397 (Accession XM\_099133). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163397. LOC203397 (Accession XM\_114695) is another VGAM1774 host target gene. LOC203397 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC203397 BINDING SITE, designated SEQ ID:43035, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59352] Another function of VGAM1774 is therefore inhibition of LOC203397 (Accession XM\_114695). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203397. LOC90499 (Accession XM\_032170) is another VGAM1774 host target gene. LOC90499 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90499 BINDING SITE, designated SEQ ID:31580, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59353] Another function of VGAM1774 is therefore inhibition of LOC90499 (Accession XM\_032170). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90499. LOC91445 (Accession XM\_018516) is another

VGAM1774 host target gene. LOC91445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91445 BINDING SITE, designated SEQ ID:30368, to the nucleotide sequence of VGAM1774 RNA, herein designated VGAM RNA, also designated SEQ ID:4485.

[59354] Another function of VGAM1774 is therefore inhibition of LOC91445 (Accession XM\_018516). Accordingly, utilities of VGAM1774 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91445. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1775 (VGAM1775) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59355] VGAM1775 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1775 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[59356] VGAM1775 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1775 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59357] VGAM1775 gene encodes a VGAM1775 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1775 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1775 precursor RNA is designated SEQ ID:1761, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1761 is located at position 994 relative to the genome of Cryphonectria Hypovirus 1.

[59358] VGAM1775 precursor RNA folds onto itself, forming VGAM1775 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59359] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1775 folded precursor RNA into VGAM1775 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 89%) nucleotide sequence of VGAM1775 RNA is designated SEQ ID:4486, and is provided hereinbelow with reference to the sequence listing part.

[59360] VGAM1775 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1775 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1775 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59361] VGAM1775 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1775 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1775 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1775 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1775 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59362] The complementary binding of VGAM1775 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1775 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1775 host target RNA into VGAM1775 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59363] It is appreciated that VGAM1775 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1775 host target genes. The mRNA of each one of this plurality of VGAM1775 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1775 RNA, herein designated VGAM RNA, and which when bound by VGAM1775 RNA causes inhibition of translation of respective one or more VGAM1775 host target proteins.

[59364] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1775 gene, herein designated VGAM GENE, on one or more VGAM1775 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59365] It is yet further appreciated that a function of VGAM1775 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGAM1775 correlate with, and may be deduced from, the identity of the host target genes which VGAM1775 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59366] Nucleotide sequences of the VGAM1775 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1775 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1775 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1775 are further described hereinbelow with reference to Table 1.

[59367] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1775 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1775 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59368] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1775 gene, herein designated VGAM is inhibition of expression of VGAM1775 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1775 correlate with, and may be deduced from, the identity of the target genes which VGAM1775 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59369] ATP-binding Cassette, Sub-family D (ALD), Member 3 (ABCD3, Accession NM\_002858) is a VGAM1775 host target gene. ABCD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCD3, corresponding to a HOST TARGET binding site



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCD3 BINDING SITE, designated SEQ ID:8753, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59370] A function of VGAM1775 is therefore inhibition of ATP-binding Cassette, Sub-family D (ALD), Member 3 (ABCD3, Accession NM\_002858), a gene which a probable transporter. Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCD3. The function of ABCD3 has been established by previous studies. Peroxisomes are single, membrane-bound, spheroid organelles present in virtually all eukaryotic cells. The polypeptide composition of the peroxisomal membrane is distinct from that of other organelles and comprises 2 quantitatively major (22K and 70K) and several minor peroxisomal membrane proteins. The peroxisome matrix contains more than 40 enzymes which are involved in a variety of metabolic processes including peroxide-based respiration, synthesis of plasmalogen and bile acids, beta-oxidation of very long chain fatty acids, and glyoxylate transamination. Biogene-

sis of peroxisomes appears to proceed by import of newly synthesized proteins into existing peroxisomes which enlarge and divide. Most matrix enzymes use an SKL (ser-lys-leu) tripeptide at the C-terminus as a targeting sequence, and the import of at least one, acyl-CoA oxidase, is ATP-dependent. Peroxisomal membrane proteins (PMP), as well as the peroxisomal matrix enzymes, are synthesized on free cytoplasmic polysomes at their mature size. Disorders with defective peroxisome biogenesis include Zellweger syndrome (ZWS1; 214100) and neonatal adrenoleukodystrophy (OMIM Ref. No. 202370). In these disorders, many peroxisomal matrix proteins are mislocated in the cytosol, whereas others, such as PMP70, PMP22 (OMIM Ref. No. 601097), and thiolase precursor, are associated with irregularly shaped vesicles which may be defective peroxisomes or peroxisome precursors. These observations led to the hypothesis that the peroxisome biogenesis defects are due to defective import mechanisms for peroxisomal matrix enzymes. Somatic cell fusion studies indicated the existence of at least 11 complementation groups for ZS and related phenotypes (Moser et al., 1995). PMP70 was mapped to chromosome 1 by analysis of somatic cell hybrid DNAs (Gartner et al.,

1992) and regionalized to 1p22–p21 by fluorescence in situ hybridization (1,2:Gartner et al., 1992, 1993). The gene encoding the mouse homolog of PMP70 (Pmp1) was located on chromosome 3 by interspecific backcross analysis.

[59371] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59372] Moser, A. B.; Rasmussen, M.; Naidu, S.; Watkins, P. A.; McGuinness, M.; Hajra, A. K.; Chen, G.; Raymond, G.; Liu, A.; Gordon, D.; Garnaas, K.; Walton, D. S.; Skjedal, O. H.; Guggenheim, M. A.; Jackson, L. G.; Elias, E. R.; Moser, H. W. : Phenotype of patients with peroxisomal disorders subdivided into sixteen complementation groups. J. Pediat. 127: 13–22, 1995. ; and

[59373] Gartner, J.; Kearns, W.; Pearson, P.; Valle, D. : Characterization and localization of the human 70–kD peroxisomal membrane protein (PMP70) gene. (Abstract) Am. J. Hum. Genet. 51 (suppl.

[59374] Further studies establishing the function and utilities of ABCD3 are found in John Hopkins OMIM database record ID 170995, and in cited publications numbered 10944–10946, 1111 and 11167–11168 listed in the bibli–

ography section hereinbelow, which are also hereby incorporated by reference. ADP-ribosylation Factor 3 (ARF3, Accession NM\_001659) is another VGAM1775 host target gene. ARF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARF3 BINDING SITE, designated SEQ ID:7381, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59375] Another function of VGAM1775 is therefore inhibition of ADP-ribosylation Factor 3 (ARF3, Accession NM\_001659). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARF3. Beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_018644) is another VGAM1775 host target gene. B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GAT1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2, designated SEQ ID:20720 and SEQ ID:27633 respectively, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59376] Another function of VGAM1775 is therefore inhibition of Beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_018644). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GAT1. Leucine Zipper, Putative Tumor Suppressor 1 (LZTS1, Accession NM\_021020) is another VGAM1775 host target gene. LZTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LZTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTS1 BINDING SITE, designated SEQ ID:22009, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59377] Another function of VGAM1775 is therefore inhibition of

Leucine Zipper, Putative Tumor Suppressor 1 (LZTS1, Accession NM\_021020), a gene which Zygin 1; may have a role in axonal outgrowth; has similarity to C. elegans UNC-76. Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTS1. The function of LZTS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM890. Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM\_003768) is another VGAM1775 host target gene. PEA15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEA15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEA15 BINDING SITE, designated SEQ ID:9852, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59378] Another function of VGAM1775 is therefore inhibition of Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM\_003768), a gene which is a phosphoprotein and

involved in glucose uptake. Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEA15. The function of PEA15 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM949. Paxillin (PXN, Accession NM\_002859) is another VGAM1775 host target gene. PXN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PXN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PXN BINDING SITE, designated SEQ ID:8756, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59379] Another function of VGAM1775 is therefore inhibition of Paxillin (PXN, Accession NM\_002859), a gene which may be involved in p53-dependent apoptosis. Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PXN. The function of PXN and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM132. Transcription Factor 7 (T-cell specific, HMG-box) (TCF7, Accession NM\_003202) is another VGAM1775 host target gene. TCF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF7 BINDING SITE, designated SEQ ID:9195, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59380] Another function of VGAM1775 is therefore inhibition of Transcription Factor 7 (T-cell specific, HMG-box) (TCF7, Accession NM\_003202). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF7. C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM\_031910) is another VGAM1775 host target gene. C1QTNF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1QTNF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or



BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QTNF6 BINDING SITE, designated SEQ ID:25658, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59381] Another function of VGAM1775 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM\_031910). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF6. DKFZp761D0614 (Accession XM\_113634) is another VGAM1775 host target gene. DKFZp761D0614 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761D0614, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761D0614 BINDING SITE, designated SEQ ID:42311, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59382] Another function of VGAM1775 is therefore inhibition of DKFZp761D0614 (Accession XM\_113634). Accordingly,

utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761D0614. FLJ10508 (Accession NM\_018118) is another VGAM1775 host target gene. FLJ10508 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10508 BINDING SITE, designated SEQ ID:19891, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59383] Another function of VGAM1775 is therefore inhibition of FLJ10508 (Accession NM\_018118). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10508. FLJ14297 (Accession NM\_024903) is another VGAM1775 host target gene. FLJ14297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14297

BINDING SITE, designated SEQ ID:24393, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59384] Another function of VGAM1775 is therefore inhibition of FLJ14297 (Accession NM\_024903). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14297. MGC11115 (Accession NM\_032310) is another VGAM1775 host target gene. MGC11115 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11115, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11115 BINDING SITE, designated SEQ ID:26096, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59385] Another function of VGAM1775 is therefore inhibition of MGC11115 (Accession NM\_032310). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11115. RAB22A, Member RAS Oncogene Family (RAB22A, Accession XM\_009454) is another VGAM1775

host target gene. RAB22A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RAB22A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB22A BINDING SITE, designated SEQ ID:30111, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59386] Another function of VGAM1775 is therefore inhibition of RAB22A, Member RAS Oncogene Family (RAB22A, Accession XM\_009454). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB22A. LOC115110 (Accession XM\_049825) is another VGAM1775 host target gene. LOC115110 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC115110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115110 BINDING SITE, designated SEQ ID:35506, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4486.

[59387] Another function of VGAM1775 is therefore inhibition of LOC115110 (Accession XM\_049825). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115110. LOC130162 (Accession XM\_059406) is another VGAM1775 host target gene. LOC130162 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130162, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130162 BINDING SITE, designated SEQ ID:36985, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59388] Another function of VGAM1775 is therefore inhibition of LOC130162 (Accession XM\_059406). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130162. LOC146375 (Accession XM\_085434) is another VGAM1775 host target gene. LOC146375 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146375, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146375 BINDING SITE, designated SEQ ID:38140, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59389] Another function of VGAM1775 is therefore inhibition of LOC146375 (Accession XM\_085434). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146375. LOC151249 (Accession XM\_010852) is another VGAM1775 host target gene. LOC151249 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151249 BINDING SITE, designated SEQ ID:30163, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59390] Another function of VGAM1775 is therefore inhibition of LOC151249 (Accession XM\_010852). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC151249. LOC153817 (Accession XM\_027964) is another VGAM1775 host target gene. LOC153817 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153817, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153817 BINDING SITE, designated SEQ ID:30599, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59391] Another function of VGAM1775 is therefore inhibition of LOC153817 (Accession XM\_027964). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153817. LOC199858 (Accession XM\_114040) is another VGAM1775 host target gene. LOC199858 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199858 BINDING SITE, designated SEQ ID:42638, to

the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59392] Another function of VGAM1775 is therefore inhibition of LOC199858 (Accession XM\_114040). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199858. LOC203378 (Accession XM\_117541) is another VGAM1775 host target gene. LOC203378 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203378, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203378 BINDING SITE, designated SEQ ID:43560, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59393] Another function of VGAM1775 is therefore inhibition of LOC203378 (Accession XM\_117541). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203378. LOC220840 (Accession XM\_165514) is another VGAM1775 host target gene. LOC220840 BINDING SITE is HOST TARGET binding site found in the 3' un-



translated region of mRNA encoded by LOC220840, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220840 BINDING SITE, designated SEQ ID:43659, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59394] Another function of VGAM1775 is therefore inhibition of LOC220840 (Accession XM\_165514). Accordingly, utilities of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220840. LOC253943 (Accession XM\_171195) is another VGAM1775 host target gene. LOC253943 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253943, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253943 BINDING SITE, designated SEQ ID:45985, to the nucleotide sequence of VGAM1775 RNA, herein designated VGAM RNA, also designated SEQ ID:4486.

[59395] Another function of VGAM1775 is therefore inhibition of LOC253943 (Accession XM\_171195). Accordingly, utilities

of VGAM1775 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253943. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1776 (VGAM1776) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59396] VGAM1776 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1776 was detected is described hereinabove with reference to Figs. 1-8.

[59397] VGAM1776 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1776 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59398] VGAM1776 gene encodes a VGAM1776 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1776 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1776 precursor RNA is designated SEQ ID:1762, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1762 is located at position 9833 relative to the genome of Cryphonectria Hypovirus 1.

[59399] VGAM1776 precursor RNA folds onto itself, forming VGAM1776 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59400] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1776 folded precursor RNA into VGAM1776 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1776 RNA is designated SEQ ID:4487, and

is provided hereinbelow with reference to the sequence listing part.

[59401] VGAM1776 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1776 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1776 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[59402] VGAM1776 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1776 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1776 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1776 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1776 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59403] The complementary binding of VGAM1776 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1776 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1776 host target RNA into VGAM1776 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59404] It is appreciated that VGAM1776 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1776 host target genes. The mRNA of each one of this plurality of VGAM1776 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1776 RNA, herein designated VGAM RNA, and which when bound by VGAM1776 RNA causes inhibition of translation of respective one or more VGAM1776 host target proteins.

[59405] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1776 gene, herein designated VGAM GENE, on one or more VGAM1776 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59406] It is yet further appreciated that a function of VGAM1776 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1776 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGAM1776 correlate with, and may be deduced from, the identity of the host target genes which VGAM1776 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59407] Nucleotide sequences of the VGAM1776 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1776 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1776 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1776 are further described hereinbelow with reference to Table 1.

[59408] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1776 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1776 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59409] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1776 gene, herein designated VGAM is inhibition of expression of VGAM1776 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1776 correlate with, and may be deduced from, the identity of the target genes which VGAM1776 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59410] Exostoses (multiple)-like 1 (EXTL1, Accession NM\_004455) is a VGAM1776 host target gene. EXTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EXTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL1 BINDING SITE, designated SEQ ID:10753, to the nucleotide sequence of VGAM1776 RNA, herein designated VGAM RNA, also designated SEQ ID:4487.

[59411] A function of VGAM1776 is therefore inhibition of Exostoses (multiple)-like 1 (EXTL1, Accession NM\_004455), a gene which probably contribute to the synthesis of heparan sulfate and heparin. Accordingly, utilities of VGAM1776 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL1.



The function of EXTL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM806. Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 4 (MLLT4, Accession XM\_051832) is another VGAM1776 host target gene. MLLT4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLLT4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT4 BINDING SITE, designated SEQ ID:35886, to the nucleotide sequence of VGAM1776 RNA, herein designated VGAM RNA, also designated SEQ ID:4487.

[59412] Another function of VGAM1776 is therefore inhibition of Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 4 (MLLT4, Accession XM\_051832), a gene which may act as an intracellular signaling component. Accordingly, utilities of VGAM1776 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT4. The function of MLLT4 and its association with various diseases

and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1608. Epiregulin (EREG, Accession NM\_001432) is another VGAM1776 host target gene. EREG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EREG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EREG BINDING SITE, designated SEQ ID:7156, to the nucleotide sequence of VGAM1776 RNA, herein designated VGAM RNA, also designated SEQ ID:4487.

[59413] Another function of VGAM1776 is therefore inhibition of Epiregulin (EREG, Accession NM\_001432). Accordingly, utilities of VGAM1776 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EREG. KIAA0057 (Accession NM\_012288) is another VGAM1776 host target gene. KIAA0057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0057 BINDING SITE, designated SEQ ID:14627, to the nucleotide sequence of VGAM1776 RNA, herein designated VGAM RNA, also designated SEQ ID:4487.

[59414] Another function of VGAM1776 is therefore inhibition of KIAA0057 (Accession NM\_012288). Accordingly, utilities of VGAM1776 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0057. KIAA1500 (Accession XM\_034353) is another VGAM1776 host target gene. KIAA1500 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1500, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1500 BINDING SITE, designated SEQ ID:32064, to the nucleotide sequence of VGAM1776 RNA, herein designated VGAM RNA, also designated SEQ ID:4487.

[59415] Another function of VGAM1776 is therefore inhibition of KIAA1500 (Accession XM\_034353). Accordingly, utilities of VGAM1776 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1500. PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM\_028335) is another

VGAM1776 host target gene. PRPF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRPF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPF8 BINDING SITE, designated SEQ ID:30686, to the nucleotide sequence of VGAM1776 RNA, herein designated VGAM RNA, also designated SEQ ID:4487.

[59416] Another function of VGAM1776 is therefore inhibition of PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM\_028335). Accordingly, utilities of VGAM1776 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRPF8. Solute Carrier Family 2 (facilitated glucose transporter), Member 12 (SLC2A12, Accession NM\_145176) is another VGAM1776 host target gene. SLC2A12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A12 BINDING SITE, designated SEQ ID:29737, to the nucleotide

sequence of VGAM1776 RNA, herein designated VGAM RNA, also designated SEQ ID:4487.

[59417] Another function of VGAM1776 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter), Member 12 (SLC2A12, Accession NM\_145176). Accordingly, utilities of VGAM1776 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A12. LOC153572 (Accession XM\_098392) is another VGAM1776 host target gene. LOC153572 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153572, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153572 BINDING SITE, designated SEQ ID:41640, to the nucleotide sequence of VGAM1776 RNA, herein designated VGAM RNA, also designated SEQ ID:4487.

[59418] Another function of VGAM1776 is therefore inhibition of LOC153572 (Accession XM\_098392). Accordingly, utilities of VGAM1776 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153572. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1777 (VGAM1777) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59419] VGAM1777 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1777 was detected is described hereinabove with reference to Figs. 1–8.

[59420] VGAM1777 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1777 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59421] VGAM1777 gene encodes a VGAM1777 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1777 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1777 precursor RNA is designated SEQ ID:1763, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1763 is located at position 7246 relative to the genome of Cryphonectria Hypovirus 1.

[59422] VGAM1777 precursor RNA folds onto itself, forming VGAM1777 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59423] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1777 folded precursor RNA into VGAM1777 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1777 RNA is designated SEQ ID:4488, and is provided hereinbelow with reference to the sequence listing part.

[59424] VGAM1777 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1777 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1777 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59425] VGAM1777 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1777 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1777 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1777 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1777 host target RNA,



herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[59426] The complementary binding of VGAM1777 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1777 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1777 host target RNA into VGAM1777 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59427] It is appreciated that VGAM1777 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1777 host target genes. The mRNA of each one of this plurality of VGAM1777 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1777 RNA, herein designated VGAM RNA, and which when bound by VGAM1777 RNA causes inhibition of translation of respective one or more

VGAM1777 host target proteins.

[59428] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1777 gene, herein designated VGAM GENE, on one or more VGAM1777 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59429] It is yet further appreciated that a function of VGAM1777 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1.

Specific functions, and accordingly utilities, of VGAM1777 correlate with, and may be deduced from, the identity of the host target genes which VGAM1777 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59430] Nucleotide sequences of the VGAM1777 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1777 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1777 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1777 are further described hereinbelow with reference to Table 1.

[59431] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1777 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1777 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59432] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1777 gene, herein designated VGAM is inhibition of expression of VGAM1777 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1777 correlate with, and may be deduced from, the identity of the target genes which VGAM1777 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59433] Glutamate Dehydrogenase 1 (GLUD1, Accession NM\_005271) is a VGAM1777 host target gene. GLUD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLUD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLUD1 BINDING SITE, designated SEQ ID:11773, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59434] A function of VGAM1777 is therefore inhibition of Glutamate Dehydrogenase 1 (GLUD1, Accession NM\_005271). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLUD1. RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM\_134422) is another VGAM1777 host target gene. RAD52 BINDING SITE1 and RAD52 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

RAD52, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD52 BINDING SITE1 and RAD52 BINDING SITE2, designated SEQ ID:28648 and SEQ ID:28656 respectively, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59435] Another function of VGAM1777 is therefore inhibition of RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM\_134422). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD52. DKFZP434O047 (Accession NM\_015594) is another VGAM1777 host target gene. DKFZP434O047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434O047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434O047 BINDING SITE, designated SEQ ID:17867, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59436] Another function of VGAM1777 is therefore inhibition of DKFZP434O047 (Accession NM\_015594). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434O047. Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295) is another VGAM1777 host target gene. EPB41L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPB41L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L1 BINDING SITE, designated SEQ ID:34942, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59437] Another function of VGAM1777 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L1. FLJ14126 (Accession NM\_024849) is another VGAM1777 host target gene. FLJ14126 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ14126, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14126 BINDING SITE, designated SEQ ID:24282, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59438] Another function of VGAM1777 is therefore inhibition of FLJ14126 (Accession NM\_024849). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14126. G Protein-coupled Receptor 107 (GPR107, Accession NM\_020960) is another VGAM1777 host target gene. GPR107 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR107, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR107 BINDING SITE, designated SEQ ID:21950, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59439] Another function of VGAM1777 is therefore inhibition of G

Protein-coupled Receptor 107 (GPR107, Accession NM\_020960). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR107. HSGP25L2G (Accession XM\_030771) is another VGAM1777 host target gene. HSGP25L2G BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSGP25L2G, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSGP25L2G BINDING SITE, designated SEQ ID:31134, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59440] Another function of VGAM1777 is therefore inhibition of HSGP25L2G (Accession XM\_030771). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSGP25L2G. Neuromedin U Receptor 2 (NMU2R, Accession NM\_020167) is another VGAM1777 host target gene. NMU2R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NMU2R, corresponding to a HOST TARGET binding site



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NMU2R BINDING SITE, designated SEQ ID:21384, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59441] Another function of VGAM1777 is therefore inhibition of Neuromedin U Receptor 2 (NMU2R, Accession NM\_020167). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NMU2R. NYD-SP11 (Accession NM\_031951) is another VGAM1777 host target gene. NYD-SP11 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NYD-SP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NYD-SP11 BINDING SITE, designated SEQ ID:25691, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59442] Another function of VGAM1777 is therefore inhibition of NYD-SP11 (Accession NM\_031951). Accordingly, utilities

of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NYD-SP11. SQV7L (Accession XM\_047287) is another VGAM1777 host target gene. SQV7L BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SQV7L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SQV7L BINDING SITE, designated SEQ ID:34932, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59443] Another function of VGAM1777 is therefore inhibition of SQV7L (Accession XM\_047287). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SQV7L. ZER6 (Accession XM\_032742) is another VGAM1777 host target gene. ZER6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZER6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZER6 BINDING SITE, designated SEQ

ID:31739, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59444] Another function of VGAM1777 is therefore inhibition of ZER6 (Accession XM\_032742). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZER6. LOC158434 (Accession XM\_098939) is another VGAM1777 host target gene. LOC158434 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158434 BINDING SITE, designated SEQ ID:41985, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59445] Another function of VGAM1777 is therefore inhibition of LOC158434 (Accession XM\_098939). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158434. LOC165741 (Accession XM\_105272) is another VGAM1777 host target gene. LOC165741 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC165741, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165741 BINDING SITE, designated SEQ ID:42189, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59446] Another function of VGAM1777 is therefore inhibition of LOC165741 (Accession XM\_105272). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165741. LOC90342 (Accession XM\_031009) is another VGAM1777 host target gene. LOC90342 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90342 BINDING SITE, designated SEQ ID:31249, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59447] Another function of VGAM1777 is therefore inhibition of

LOC90342 (Accession XM\_031009). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90342. LOC92689 (Accession XM\_046663) is another VGAM1777 host target gene. LOC92689 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92689, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92689 BINDING SITE, designated SEQ ID:34780, to the nucleotide sequence of VGAM1777 RNA, herein designated VGAM RNA, also designated SEQ ID:4488.

[59448] Another function of VGAM1777 is therefore inhibition of LOC92689 (Accession XM\_046663). Accordingly, utilities of VGAM1777 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92689. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1778 (VGAM1778) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[59449] VGAM1778 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1778 was detected is described hereinabove with reference to Figs. 1–8.

[59450] VGAM1778 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1778 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59451] VGAM1778 gene encodes a VGAM1778 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1778 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1778 precursor RNA is designated SEQ ID:1764, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1764 is located at position 3023 relative to the genome of Cryphonectria Hypovirus 1.

[59452] VGAM1778 precursor RNA folds onto itself, forming VGAM1778 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59453] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1778 folded precursor RNA into VGAM1778 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1778 RNA is designated SEQ ID:4489, and is provided hereinbelow with reference to the sequence listing part.

[59454] VGAM1778 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1778 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1778 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[59455] VGAM1778 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1778 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1778 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1778 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1778 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR



and 5`UTR regions.

[59456] The complementary binding of VGAM1778 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1778 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1778 host target RNA into VGAM1778 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59457] It is appreciated that VGAM1778 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1778 host target genes. The mRNA of each one of this plurality of VGAM1778 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1778 RNA, herein designated VGAM RNA, and which when bound by VGAM1778 RNA causes inhibition of translation of respective one or more VGAM1778 host target proteins.

[59458] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1778 gene, herein designated VGAM GENE, on one

or more VGAM1778 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59459] It is yet further appreciated that a function of VGAM1778 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1778 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGAM1778 correlate with, and may be deduced from, the identity of the host target genes which VGAM1778 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59460] Nucleotide sequences of the VGAM1778 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1778 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1778 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1778 are further described hereinbelow with reference to Table 1.

[59461] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1778 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1778 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59462] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1778 gene, herein designated VGAM is inhibition of expression of VGAM1778 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1778 correlate with, and may be deduced from, the identity of the target genes which VGAM1778 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59463] DnaJ (Hsp40) Homolog, Subfamily B, Member 1 (DNAJB1,

Accession NM\_006145) is a VGAM1778 host target gene. DNAJB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJB1 BINDING SITE, designated SEQ ID:12788, to the nucleotide sequence of VGAM1778 RNA, herein designated VGAM RNA, also designated SEQ ID:4489.

[59464] A function of VGAM1778 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily B, Member 1 (DNAJB1, Accession NM\_006145), a gene which may prevent aggregation of newly translated proteins. Accordingly, utilities of VGAM1778 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJB1. The function of DNAJB1 has been established by previous studies. The E. coli heat-shock protein DnaJ (see OMIM Ref. No. 140550) functions together with DnaK (HSPA1A; 140550) and GrpE (OMIM Ref. No. 606173) as a molecular chaperone, involving them in assembly and disassembly of protein complexes, protein folding, renaturation of denatured proteins, prevention of protein aggre-

gation, and protein export. By screening a human placenta cDNA library with anti-hsp40 antibody, Ohtsuka (1993) isolated a cDNA encoding a 40-kD heat-shock protein designated HSPF1. The deduced 340-amino acid HSPF1 protein is 34% identical to E. coli DnaJ and 34% and 36% identical to HSJ1 (OMIM Ref. No. 604139) and HSJ2 (OMIM Ref. No. 602837), respectively. By Northern blot analysis, Hata and Ohtsuka (1998) showed that expression of a major 2.4-kb and a minor 1.4-kb HSPF1 transcript is drastically induced by heat shock. Several dominant human neurodegenerative diseases involve the expansion of a polyglutamine within the disease proteins. This expansion confers toxicity on the proteins and is associated with nuclear inclusion formation. Data indicate that molecular chaperones can modulate polyglutamine pathogenesis. To elucidate the basis of polyglutamine toxicity and the mechanism by which chaperones suppress neurodegeneration, Chan et al. (2000) studied transgenic Drosophila disease models of Machado-Joseph disease (OMIM Ref. No. 109150) and Huntington disease (OMIM Ref. No. 143100). They demonstrated that Hsp70 (see OMIM Ref. No. 140559) and Hdj1, the Drosophila homolog to human HSP40 (see OMIM Ref. No. 604139), showed

substrate specificity for polyglutamine proteins as well as synergy in suppression of neurotoxicity, and altered the solubility properties of the mutant polyglutamine protein.

[59465] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59466] Chan, H. Y. E.; Warrick, J. M.; Gray-Board, G. L.; Paulson, H. L.; Bonini, N. M. : Mechanisms of chaperone suppression of polyglutamine disease: selectivity, synergy and modulation of protein solubility in *Drosophila*. *Hum. Molec. Genet.* 9: 2811–2820, 2000. ; and

[59467] Hata, M.; Ohtsuka, K. : Characterization of HSE sequences in human Hsp40 gene: structural and promoter analysis. *Biochim. Biophys. Acta* 1397: 43–55, 1998.

[59468] Further studies establishing the function and utilities of DNAJB1 are found in John Hopkins OMIM database record ID 604572, and in cited publications numbered 522 and 7947–7949 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. G Protein-coupled Receptor 75 (GPR75, Accession NM\_006794) is another VGAM1778 host target gene. GPR75 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GPR75, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR75 BINDING SITE, designated SEQ ID:13669, to the nucleotide sequence of VGAM1778 RNA, herein designated VGAM RNA, also designated SEQ ID:4489.

[59469] Another function of VGAM1778 is therefore inhibition of G Protein-coupled Receptor 75 (GPR75, Accession NM\_006794). Accordingly, utilities of VGAM1778 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR75. Hermansky-Pudlak Syndrome 1 (HPS1, Accession NM\_000195) is another VGAM1778 host target gene. HPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPS1 BINDING SITE, designated SEQ ID:5693, to the nucleotide sequence of VGAM1778 RNA, herein designated VGAM RNA, also designated SEQ ID:4489.

[59470] Another function of VGAM1778 is therefore inhibition of Hermansky-Pudlak Syndrome 1 (HPS1, Accession

NM\_000195). Accordingly, utilities of VGAM1778 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPS1. Heparan Sulfate (glucosamine) 3-O-sulfotransferase 3A1 (HS3ST3A1, Accession NM\_006042) is another VGAM1778 host target gene. HS3ST3A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HS3ST3A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS3ST3A1 BINDING SITE, designated SEQ ID:12676, to the nucleotide sequence of VGAM1778 RNA, herein designated VGAM RNA, also designated SEQ ID:4489.

[59471] Another function of VGAM1778 is therefore inhibition of Heparan Sulfate (glucosamine) 3-O-sulfotransferase 3A1 (HS3ST3A1, Accession NM\_006042), a gene which plays a role in the generation of heparan sulfate proteoglycan. Accordingly, utilities of VGAM1778 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS3ST3A1. The function of HS3ST3A1 and its association with various diseases and clinical conditions, has been established by previous stud-



ies, as described hereinabove with reference to VGAM1454.RalA Binding Protein 1 (RALBP1, Accession NM\_006788) is another VGAM1778 host target gene. RALBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RALBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RALBP1 BINDING SITE, designated SEQ ID:13664, to the nucleotide sequence of VGAM1778 RNA, herein designated VGAM RNA, also designated SEQ ID:4489.

[59472] Another function of VGAM1778 is therefore inhibition of RalA Binding Protein 1 (RALBP1, Accession NM\_006788), a gene which plays a role in signal transduction and catalyzes the transport of glutathione conjugates and xenobiotics. Accordingly, utilities of VGAM1778 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RALBP1. The function of RALBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM345.Transient Receptor Potential Cation Channel,

Subfamily V, Member 1 (TRPV1, Accession NM\_080705) is another VGAM1778 host target gene. TRPV1 BINDING SITE1 through TRPV1 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRPV1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPV1 BINDING SITE1 through TRPV1 BINDING SITE4, designated SEQ ID:27999, SEQ ID:28007, SEQ ID:20811 and SEQ ID:27991 respectively, to the nucleotide sequence of VGAM1778 RNA, herein designated VGAM RNA, also designated SEQ ID:4489.

[59473] Another function of VGAM1778 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily V, Member 1 (TRPV1, Accession NM\_080705), a gene which functions as a receptor for capsaicin. Accordingly, utilities of VGAM1778 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPV1. The function of TRPV1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM146.LOC219649 (Accession XM\_167562) is another VGAM1778 host target gene.

LOC219649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219649 BINDING SITE, designated SEQ ID:44669, to the nucleotide sequence of VGAM1778 RNA, herein designated VGAM RNA, also designated SEQ ID:4489.

[59474] Another function of VGAM1778 is therefore inhibition of LOC219649 (Accession XM\_167562). Accordingly, utilities of VGAM1778 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219649. LOC91828 (Accession XM\_040910) is another VGAM1778 host target gene. LOC91828 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91828 BINDING SITE, designated SEQ ID:33408, to the nucleotide sequence of VGAM1778 RNA, herein designated VGAM RNA, also designated SEQ ID:4489.

[59475] Another function of VGAM1778 is therefore inhibition of LOC91828 (Accession XM\_040910). Accordingly, utilities of VGAM1778 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91828. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1779 (VGAM1779) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59476] VGAM1779 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1779 was detected is described hereinabove with reference to Figs. 1–8.

[59477] VGAM1779 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1779 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59478] VGAM1779 gene encodes a VGAM1779 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1779 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1779 precursor RNA is designated SEQ ID:1765, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1765 is located at position 4059 relative to the genome of Cryphonectria Hypovirus 1.

[59479] VGAM1779 precursor RNA folds onto itself, forming VGAM1779 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59480] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1779 folded precursor RNA into VGAM1779 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1779 RNA is designated SEQ ID:4490, and is provided hereinbelow with reference to the sequence listing part.

[59481] VGAM1779 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1779 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1779 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[59482] VGAM1779 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1779 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1779 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1779 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1779 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59483] The complementary binding of VGAM1779 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1779 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1779 host target RNA into VGAM1779 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59484] It is appreciated that VGAM1779 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1779 host target genes. The mRNA of each one of this plurality of VGAM1779 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1779 RNA, herein designated VGAM RNA, and which when bound by VGAM1779 RNA causes inhibition of translation of respective one or more VGAM1779 host target proteins.

[59485] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1779 gene, herein designated VGAM GENE, on one or more VGAM1779 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).



[59486] It is yet further appreciated that a function of VGAM1779 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1779 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGAM1779 correlate with, and may be deduced from, the identity of the host target genes which VGAM1779 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59487] Nucleotide sequences of the VGAM1779 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1779 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1779 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1779 are further described hereinbelow with reference to Table 1.

[59488] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1779 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1779 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[59489] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1779 gene, herein designated VGAM is inhibition of expression of VGAM1779 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1779 correlate with, and may be deduced from, the identity of the target genes which VGAM1779 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59490] Carcinoembryonic Antigen-related Cell Adhesion Molecule 6 (non-specific cross reacting antigen) (CEACAM6, Accession NM\_002483) is a VGAM1779 host target gene. CEACAM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CEACAM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEACAM6 BINDING SITE, designated SEQ ID:8309, to the nucleotide sequence of VGAM1779 RNA, herein designated VGAM RNA, also designated SEQ ID:4490.

[59491] A function of VGAM1779 is therefore inhibition of Carcinoembryonic Antigen-related Cell Adhesion Molecule 6

(non-specific cross reacting antigen) (CEACAM6, Accession NM\_002483), a gene which Non-specific cross reacting antigen (. Accordingly, utilities of VGAM1779 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEACAM6. The function of CEACAM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM286. Trichorhinophalangeal Syndrome I (TRPS1, Accession NM\_014112) is another VGAM1779 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15351, to the nucleotide sequence of VGAM1779 RNA, herein designated VGAM RNA, also designated SEQ ID:4490.

[59492] Another function of VGAM1779 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM\_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of

VGAM1779 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Actin Related Protein 2/3 Complex, Subunit 5, 16kDa (ARPC5, Accession NM\_005717) is another VGAM1779 host target gene. ARPC5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARPC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARPC5 BINDING SITE, designated SEQ ID:12272, to the nucleotide sequence of VGAM1779 RNA, herein designated VGAM RNA, also designated SEQ ID:4490.

[59493] Another function of VGAM1779 is therefore inhibition of Actin Related Protein 2/3 Complex, Subunit 5, 16kDa (ARPC5, Accession NM\_005717). Accordingly, utilities of VGAM1779 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARPC5. FLJ23056 (Accession NM\_024582) is another VGAM1779 host target gene. FLJ23056 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by FLJ23056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23056 BINDING SITE, designated SEQ ID:23808, to the nucleotide sequence of VGAM1779 RNA, herein designated VGAM RNA, also designated SEQ ID:4490.

[59494] Another function of VGAM1779 is therefore inhibition of FLJ23056 (Accession NM\_024582). Accordingly, utilities of VGAM1779 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23056. LOC51141 (Accession XM\_043953) is another VGAM1779 host target gene. LOC51141 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51141, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51141 BINDING SITE, designated SEQ ID:34048, to the nucleotide sequence of VGAM1779 RNA, herein designated VGAM RNA, also designated SEQ ID:4490.

[59495] Another function of VGAM1779 is therefore inhibition of

LOC51141 (Accession XM\_043953). Accordingly, utilities of VGAM1779 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51141. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1780 (VGAM1780) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59496] VGAM1780 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1780 was detected is described hereinabove with reference to Figs. 1-8.

[59497] VGAM1780 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1780 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59498] VGAM1780 gene encodes a VGAM1780 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1780 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1780 precursor RNA is designated SEQ ID:1766, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1766 is located at position 6807 relative to the genome of Cryphonectria Hypovirus 1.

- [59499] VGAM1780 precursor RNA folds onto itself, forming VGAM1780 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [59500] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1780 folded precursor RNA into VGAM1780 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide se-

quence of VGAM1780 RNA is designated SEQ ID:4491, and is provided hereinbelow with reference to the sequence listing part.

[59501] VGAM1780 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1780 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1780 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59502] VGAM1780 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1780 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1780 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is



meant as an illustration only, and is not meant to be limiting – VGAM1780 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1780 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59503] The complementary binding of VGAM1780 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1780 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1780 host target RNA into VGAM1780 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59504] It is appreciated that VGAM1780 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1780 host target genes. The mRNA of each one of this plurality of VGAM1780 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1780 RNA, herein designated VGAM RNA, and which when bound by VGAM1780 RNA causes inhibition of translation of respective one or more VGAM1780 host target proteins.

[59505] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1780 gene, herein designated VGAM GENE, on one or more VGAM1780 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59506] It is yet further appreciated that a function of VGAM1780

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1780 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGAM1780 correlate with, and may be deduced from, the identity of the host target genes which VGAM1780 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59507] Nucleotide sequences of the VGAM1780 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1780 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1780 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1780 are further described hereinbelow with reference to Table 1.

[59508] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1780 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1780 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59509] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1780 gene, herein designated VGAM is inhibition of expression of VGAM1780 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1780 correlate with, and may be deduced from, the identity of the target genes which VGAM1780 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59510] Leucine Zipper, Putative Tumor Suppressor 1 (LZTS1, Accession NM\_021020) is a VGAM1780 host target gene. LZTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LZTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTS1 BINDING SITE, designated SEQ ID:22005, to the nucleotide sequence of VGAM1780 RNA, herein designated VGAM RNA, also designated SEQ ID:4491.

[59511] A function of VGAM1780 is therefore inhibition of Leucine Zipper, Putative Tumor Suppressor 1 (LZTS1, Accession NM\_021020), a gene which Zygin 1; may have a role in axonal outgrowth; has similarity to C. elegans UNC-76.

Accordingly, utilities of VGAM1780 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTS1. The function of LZTS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM890. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1781 (VGAM1781) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59512] VGAM1781 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1781 was detected is described hereinabove with reference to Figs. 1–8.

[59513] VGAM1781 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1781 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59514] VGAM1781 gene encodes a VGAM1781 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1781 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1781 precursor RNA is designated SEQ ID:1767, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1767 is located at position 9633 relative to the genome of Cryphonectria Hypovirus 1.

- [59515] VGAM1781 precursor RNA folds onto itself, forming VGAM1781 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [59516] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1781 folded precursor RNA into VGAM1781 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1781 RNA is designated SEQ ID:4492, and is provided hereinbelow with reference to the sequence listing part.

[59517] VGAM1781 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1781 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1781 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59518] VGAM1781 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1781 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1781 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1781 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1781 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59519] The complementary binding of VGAM1781 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1781 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1781 host target RNA into VGAM1781 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59520] It is appreciated that VGAM1781 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1781 host target genes. The mRNA of



each one of this plurality of VGAM1781 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1781 RNA, herein designated VGAM RNA, and which when bound by VGAM1781 RNA causes inhibition of translation of respective one or more VGAM1781 host target proteins.

[59521] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1781 gene, herein designated VGAM GENE, on one or more VGAM1781 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[59522] It is yet further appreciated that a function of VGAM1781 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGAM1781 correlate with, and may be deduced from, the identity of the host target genes which VGAM1781 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59523] Nucleotide sequences of the VGAM1781 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1781 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1781 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1781 are further described hereinbelow with reference to Table 1.

[59524] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1781 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1781 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59525] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1781 gene, herein designated VGAM is inhibition of expression of VGAM1781 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1781 correlate with, and may be deduced from, the identity of the target genes which VGAM1781 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59526] Centrosomal Protein 2 (CEP2, Accession NM\_006779) is a VGAM1781 host target gene. CEP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CEP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP2 BINDING SITE, designated SEQ ID:13650, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59527] A function of VGAM1781 is therefore inhibition of Centrosomal Protein 2 (CEP2, Accession NM\_006779), a gene which interacts with TC10 and CDC42. Accordingly, utili-

ties of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEP2. The function of CEP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM329. CERD4 (Accession NM\_012074) is another VGAM1781 host target gene. CERD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CERD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CERD4 BINDING SITE, designated SEQ ID:14344, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59528] Another function of VGAM1781 is therefore inhibition of CERD4 (Accession NM\_012074). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CERD4. Glucokinase (hexokinase 4, maturity onset diabetes of the young 2) (GCK, Accession NM\_000162) is another VGAM1781 host target gene. GCK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by GCK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCK BINDING SITE, designated SEQ ID:5670, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59529] Another function of VGAM1781 is therefore inhibition of Glucokinase (hexokinase 4, maturity onset diabetes of the young 2) (GCK, Accession NM\_000162), a gene which catalyzes the initial step in utilization of glucose by the beta-cell and liver at physiological glucose concentration. Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCK. The function of GCK has been established by previous studies. B lymphocytes that reside in the germinal center of lymphoid follicles are functionally and phenotypically distinct from those residing in the surrounding mantle zone. Various regulatory and structural genes control a complex series of differentiation and selection steps through which B cells that exit the germinal center of lymphoid follicles must pass. In differential hybridization studies to identify some of these genes, Katz

et al. (1994) isolated a novel gene based on its preferential expression in tonsillar germinal center B lymphocytes. The complete nucleotide sequence predicted a 819-amino acid protein, named GC (for 'germinal center') kinase, with homology to serine-threonine protein kinases. Its catalytic domain was 39% and 37% identical to those of *S. cerevisiae* STE20 and *Drosophila* NinaC proteins, respectively. Northern blot analysis revealed expression of a 2.9-kb mRNA in several human tissues, including brain, lung, and placenta. In situ hybridization of tonsil tissue demonstrated preferential hybridization to the germinal center region. The expressed protein phosphorylated casein and myelin basic protein in in vitro kinase assays. Pombo et al. (1995) showed that GC kinase, or GCK, specifically activates the SAPK (OMIM Ref. No. 601335) pathway. They also showed that GCK is activated in situ by TNF- $\alpha$  (OMIM Ref. No. 191160), a potent SAPK agonist. The authors suggested that the SAPK pathway may be active in the differentiation and selection of B cells in the germinal center

[59530] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [59531] Katz, P.; Whalen, G.; Kehrl, J. H. : Differential expression of a novel protein kinase in human B lymphocytes: preferential localization in the germinal center. J. Biol. Chem. 269: 16802–16809, 1994. ; and
- [59532] Ren, M.; Zeng, J.; De Lemos–Chiarandini, C.; Rosenfeld, M.; Adesnik, M.; Sabatini, D. D. : In its active form, the GTP–binding protein rab8 interacts with a stress–activated protein kina.
- [59533] Further studies establishing the function and utilities of GCK are found in John Hopkins OMIM database record ID 603166, and in cited publications numbered 11498–5866 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM\_085943) is another VGAM1781 host target gene. GRLF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GRLF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRLF1 BINDING SITE, designated SEQ ID:38413, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ

ID:4492.

[59534] Another function of VGAM1781 is therefore inhibition of Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM\_085943), a gene which inhibits transcription of the glucocorticoid receptor gene. Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRLF1. The function of GRLF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Human Immunodeficiency Virus Type I Enhancer Binding Protein 3 (HIVEP3, Accession NM\_024503) is another VGAM1781 host target gene. HIVEP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HIVEP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIVEP3 BINDING SITE, designated SEQ ID:23698, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59535] Another function of VGAM1781 is therefore inhibition of



Human Immunodeficiency Virus Type I Enhancer Binding Protein 3 (HIVEP3, Accession NM\_024503), a gene which is required for transcriptional activation of glucose- re-pressible alcohol dehydrogenase (adh2). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIVEP3. The function of HIVEP3 has been established by previous studies. Hicar et al. (2001) cloned HIVEP3, a member of the HIVEP family (see OMIM Ref. No. HIVEP1; 194540). HIVEPs encode large zinc finger proteins and regulate transcription via the kappa-B enhancer motif. HIVEP3 is homologous to the mouse Krc (kappa-B-binding and recognition component of the V(D)J recombination signal sequence) protein. The largest open reading frame of HIVEP3 contains 2,406 amino acids and is 80% identical to Krc. RNA studies showed that multiple HIVEP3 transcripts are differentially expressed and regulated. Transcription termination occurs in the ultimate exon, exon 10, or in exon 6. Therefore, HIVEP3 may produce protein isoforms that contain or exclude the C-terminal DNA-binding domain and the leucine zipper by alternative RNA splicing and differential polyadenylation. GENE FUNCTION Oukka et al. (2002) described a function for the zinc fin-

ger transcription factor Krc in regulating patterns of gene activation in response to proinflammatory stimuli. Krc overexpression inhibited, while antisense or dominant-negative Krc enhanced, NF-kappa-B (OMIM Ref. No. 164011)-dependent transactivation and JNK (OMIM Ref. No. 601158) phosphorylation and consequently inhibited apoptosis and cytokine gene expression. The effect of Krc was mediated through its interaction with the adaptor protein TRAF2 (OMIM Ref. No. 601895). Oukka et al. (2002) concluded that Krc is a participant in the signal transduction pathway leading from the TNF receptor (see OMIM Ref. No. 602746) to gene activation and may play a critical role in inflammatory and apoptotic responses.

[59536] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59537] Hicar, M. D.; Liu, Y.; Allen, C. E.; Wu, L.-C. : Structure of the human zinc finger protein HIVEP3: molecular cloning, expression, exon-intron structure, and comparison with paralogous genes HIVEP1 and HIVEP2. *Genomics* 71: 89-100, 2001. ; and

[59538] Oukka, M.; Kim, S. T.; Lugo, G.; Sun, J.; Wu, L.-C.; Glimcher, L. H. : A mammalian homolog of *Drosophila*

schnurri, KRC, regulates TNF receptor-driven responses and interacts with TRAF2.

[59539] Further studies establishing the function and utilities of HIVEP3 are found in John Hopkins OMIM database record ID 606649, and in cited publications numbered 613 and 6144 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prostaglandin F Receptor (FP) (PTGFR, Accession NM\_000959) is another VGAM1781 host target gene. PTGFR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGFR BINDING SITE, designated SEQ ID:6661, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59540] Another function of VGAM1781 is therefore inhibition of Prostaglandin F Receptor (FP) (PTGFR, Accession NM\_000959), a gene which mediates intracellular calcium flux, strongly similar to murine Ptgfr. Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PTGFR. The function of PTGFR has been established by previous studies. Prostaglandin F(2- $\alpha$ ) is involved in a number of physiologic processes. It serves as a potent luteolytic agent in many species, has been implicated as a modulator of intraocular pressure, and may be important in smooth muscle contraction in the uterus and elsewhere. Its effects on cells are mediated through specific interaction with prostaglandin receptors. Abramovitz et al.

(1994) cloned a cDNA encoding the human prostanoid FP receptor from a uterus cDNA library. The 359-amino acid protein has 7 putative transmembrane domains characteristic of the G protein-coupled receptors. As expected, expression studies of the cDNA in *Xenopus* oocytes and COS cells showed strongest binding to PGF(2- $\alpha$ ). Subsequently, Duncan et al. (1995) mapped the gene to 1p31.1 by in situ hybridization. Using a panel of interspecific backcross mice, Ishikawa et al. (1996) mapped the *Ptgfr* gene to distal mouse chromosome 3. Sugimoto et al. (1997) showed that knockout mice lacking the receptor for prostaglandin F(2- $\alpha$ ) are unable to deliver normal fetuses at term due to a lack of response to oxytocin. The mice also failed to show the decline in serum progesterone expected to precede parturition. However, if the

mice had their ovaries removed at day 19 of pregnancy, normal delivery occurred. The authors concluded that parturition is initiated when prostaglandin F(2- $\alpha$ ) interacts with its receptor in ovarian luteal cells to induce luteolysis. Sugimoto et al. (1997) also suggested that this mechanism may explain why aspirin-like drugs delay parturition.

[59541] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59542] Sugimoto, Y.; Yamasaki, A.; Segi, E.; Tsuboi, K.; Aze, Y.; Nishimura, T.; Oida, H.; Yoshida, N.; Tanaka, T.; Katsuyama, M.; Hasumoto, K.; Murata, T.; Hirata, M.; Ushikubi, F.; Negishi, M.; Ichikawa, A.; Narumiya, S. : Failure of parturition in mice lacking the prostaglandin F receptor. *Science* 277: 681–683, 1997. ; and

[59543] Ishikawa, T.; Tamai, Y.; Rochelle, J. M.; Hirata, M.; Namba, T.; Sugimoto, Y.; Ichikawa, A.; Narumiya, S.; Taketo, M. M.; Seldin, M. F. : Mapping of the genes encoding mouse prostaglandi.

[59544] Further studies establishing the function and utilities of PTGFR are found in John Hopkins OMIM database record ID 600563, and in cited publications numbered 8166–816

and 10839 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM\_005063) is another VGAM1781 host target gene. SCD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SCD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCD BINDING SITE, designated SEQ ID:11489, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59545] Another function of VGAM1781 is therefore inhibition of Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM\_005063), a gene which functions in the synthesis of unsaturated fatty acids. Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCD. The function of SCD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM314. Transmembrane 4 Superfamily Member 6 (TM4SF6, Accession NM\_003270) is another VGAM1781

host target gene. TM4SF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TM4SF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TM4SF6 BINDING SITE, designated SEQ ID:9284, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59546] Another function of VGAM1781 is therefore inhibition of Transmembrane 4 Superfamily Member 6 (TM4SF6, Accession NM\_003270), a gene which plays a role in the regulation of cell development, activation, growth and motility. Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TM4SF6. The function of TM4SF6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM84.13CDNA73 (Accession NM\_023037) is another VGAM1781 host target gene. 13CDNA73 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by 13CDNA73, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of 13CDNA73 BINDING SITE, designated SEQ ID:23321, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59547] Another function of VGAM1781 is therefore inhibition of 13CDNA73 (Accession NM\_023037). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with 13CDNA73. Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM\_017575) is another VGAM1781 host target gene. C17orf31 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C17orf31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf31 BINDING SITE, designated SEQ ID:19002, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59548] Another function of VGAM1781 is therefore inhibition of Chromosome 17 Open Reading Frame 31 (C17orf31, Ac-



cession NM\_017575). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf31.

FLJ13241 (Accession NM\_025088) is another VGAM1781 host target gene. FLJ13241 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13241 BINDING SITE, designated SEQ ID:24706, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59549] Another function of VGAM1781 is therefore inhibition of FLJ13241 (Accession NM\_025088). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13241. FLJ14743 (Accession XM\_042708) is another VGAM1781 host target gene. FLJ14743 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ14743 BINDING SITE, designated SEQ ID:33762, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59550] Another function of VGAM1781 is therefore inhibition of FLJ14743 (Accession XM\_042708). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14743. GMPPB (Accession XM\_171044) is another VGAM1781 host target gene. GMPPB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GMPPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GMPPB BINDING SITE, designated SEQ ID:45811, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59551] Another function of VGAM1781 is therefore inhibition of GMPPB (Accession XM\_171044). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMPPB. KIAA0445 (Accession NM\_014675) is another VGAM1781

host target gene. KIAA0445 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0445 BINDING SITE, designated SEQ ID:16146, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59552] Another function of VGAM1781 is therefore inhibition of KIAA0445 (Accession NM\_014675). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0445. KIAA0478 (Accession NM\_014870) is another VGAM1781 host target gene. KIAA0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0478 BINDING SITE, designated SEQ ID:16976, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59553] Another function of VGAM1781 is therefore inhibition of KIAA0478 (Accession NM\_014870). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0478. KIAA1018 (Accession NM\_014967) is another VGAM1781 host target gene. KIAA1018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1018 BINDING SITE, designated SEQ ID:17356, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59554] Another function of VGAM1781 is therefore inhibition of KIAA1018 (Accession NM\_014967). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1018. MGC2477 (Accession NM\_024099) is another VGAM1781 host target gene. MGC2477 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2477, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2477 BINDING SITE, designated SEQ ID:23541, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59555] Another function of VGAM1781 is therefore inhibition of MGC2477 (Accession NM\_024099). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2477. Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM\_080792) is another VGAM1781 host target gene. PTPNS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPNS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPNS1 BINDING SITE, designated SEQ ID:28052, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59556] Another function of VGAM1781 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM\_080792). Accordingly,

utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPNS1. Tigger Transposable Element Derived 5 (TIGD5, Accession NM\_032862) is another VGAM1781 host target gene. TIGD5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TIGD5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIGD5 BINDING SITE, designated SEQ ID:26667, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59557] Another function of VGAM1781 is therefore inhibition of Tigger Transposable Element Derived 5 (TIGD5, Accession NM\_032862). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIGD5. Thyroid Hormone Receptor Interactor 13 (TRIP13, Accession NM\_004237) is another VGAM1781 host target gene. TRIP13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIP13, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIP13 BINDING SITE, designated SEQ ID:10435, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59558] Another function of VGAM1781 is therefore inhibition of Thyroid Hormone Receptor Interactor 13 (TRIP13, Accession NM\_004237). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIP13. LOC115110 (Accession XM\_049825) is another VGAM1781 host target gene. LOC115110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115110 BINDING SITE, designated SEQ ID:35508, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59559] Another function of VGAM1781 is therefore inhibition of LOC115110 (Accession XM\_049825). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC115110. LOC149579 (Accession XM\_048743) is another VGAM1781 host target gene. LOC149579 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149579, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149579 BINDING SITE, designated SEQ ID:35242, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59560] Another function of VGAM1781 is therefore inhibition of LOC149579 (Accession XM\_048743). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149579. LOC154386 (Accession XM\_087920) is another VGAM1781 host target gene. LOC154386 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC154386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154386 BINDING SITE, designated SEQ ID:39471, to



the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59561] Another function of VGAM1781 is therefore inhibition of LOC154386 (Accession XM\_087920). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154386. LOC256158 (Accession XM\_175125) is another VGAM1781 host target gene. LOC256158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE, designated SEQ ID:46624, to the nucleotide sequence of VGAM1781 RNA, herein designated VGAM RNA, also designated SEQ ID:4492.

[59562] Another function of VGAM1781 is therefore inhibition of LOC256158 (Accession XM\_175125). Accordingly, utilities of VGAM1781 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256158. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1782 (VGAM1782) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59563] VGAM1782 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1782 was detected is described hereinabove with reference to Figs. 1–8.

[59564] VGAM1782 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 1. VGAM1782 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59565] VGAM1782 gene encodes a VGAM1782 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1782 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1782 precursor RNA is designated SEQ ID:1768, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1768 is located at position 9154 relative to the genome of Cryphonectria Hypovirus 1.

[59566] VGAM1782 precursor RNA folds onto itself, forming VGAM1782 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59567] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1782 folded precursor RNA into VGAM1782 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1782 RNA is designated SEQ ID:4493, and is provided hereinbelow with reference to the sequence listing part.

[59568] VGAM1782 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1782 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1782 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[59569] VGAM1782 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1782 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1782 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1782 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1782 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59570] The complementary binding of VGAM1782 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1782 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1782 host target RNA into VGAM1782 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59571] It is appreciated that VGAM1782 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1782 host target genes. The mRNA of each one of this plurality of VGAM1782 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1782 RNA, herein designated VGAM RNA, and which when bound by VGAM1782 RNA causes inhibition of translation of respective one or more VGAM1782 host target proteins.

[59572] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1782 gene, herein designated VGAM GENE, on one or more VGAM1782 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59573] It is yet further appreciated that a function of VGAM1782 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1782 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGAM1782 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1782 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59574] Nucleotide sequences of the VGAM1782 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1782 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1782 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1782 are further described hereinbelow with reference to Table 1.

[59575] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1782 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1782 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59576] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1782 gene, herein designated VGAM is inhibition of expression of VGAM1782 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1782 correlate with, and may be deduced from, the identity of the target genes which VGAM1782

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59577] Breast Cancer 1, Early Onset (BRCA1, Accession NM\_007294) is a VGAM1782 host target gene. BRCA1 BINDING SITE1 through BRCA1 BINDING SITE10 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BRCA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRCA1 BINDING SITE1 through BRCA1 BINDING SITE10, designated SEQ ID:14164, SEQ ID:14201, SEQ ID:14189, SEQ ID:14209, SEQ ID:14221, SEQ ID:14195, SEQ ID:14170, SEQ ID:14182, SEQ ID:14215 and SEQ ID:14176 respectively, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59578] A function of VGAM1782 is therefore inhibition of Breast Cancer 1, Early Onset (BRCA1, Accession NM\_007294). Accordingly, utilities of VGAM1782 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRCA1. Heat Shock 70kDa Protein 5 (glucose-regulated protein, 78kDa) (HSPA5, Accession NM\_005347) is another VGAM1782 host target gene.



HSPA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPA5 BINDING SITE, designated SEQ ID:11820, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59579] Another function of VGAM1782 is therefore inhibition of Heat Shock 70kDa Protein 5 (glucose-regulated protein, 78kDa) (HSPA5, Accession NM\_005347), a gene which is involved in the folding and assembly of proteins in the endoplasmic reticulum (ER). Accordingly, utilities of VGAM1782 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPA5. The function of HSPA5 has been established by previous studies. Hendershot et al. (1994) pointed out that GRP78, also referred to as 'immunoglobulin heavy chain-binding protein' (BiP), is a member of the heat-shock protein-70 (HSP70) family and is involved in the folding and assembly of proteins in the endoplasmic reticulum (ER). Because so many ER proteins interact with GRP78 transiently, it may

play a key role in monitoring protein transport through the cell. To examine how the binding of BiP influences the conformational maturation of thyroglobulin (TG; 188450), Muresan and Arvan (1998) expressed TG in Chinese hamster ovary (CHO) cells genetically manipulated for selectively increased BiP expression (CHO-B cells). The TG expressed in CHO-B cells did not contain any mutations that induce misfolding (i.e., no unfolded protein response), so that levels of all other ER chaperones were normal. Increased availability of BiP did not accelerate TG secretion; rather, the export of newly synthesized TG was delayed. TG that was detained intracellularly was concentrated in the ER. Muresan and Arvan (1998) concluded that increased binding of BiP to TG leads to its delayed conformational maturation in the ER.

[59580] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59581] Hendershot, L. M.; Valentine, V. A.; Lee, A. S.; Morris, S. W.; Shapiro, D. N. : Localization of the gene encoding human BiP/GRP78, the endoplasmic reticulum cognate of the HSP70 family, to chromosome 9q34. *Genomics* 20: 281-284, 1994. ; and

[59582] Muresan, Z.; Arvan, P. : Enhanced binding to the molecular chaperone BiP slows thyroglobulin export from the endoplasmic reticulum. *Molec. Endocr.* 12: 458–467, 1998.

[59583] Further studies establishing the function and utilities of HSPA5 are found in John Hopkins OMIM database record ID 138120, and in cited publications numbered 1696–170 and 12097 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prostaglandin I<sub>2</sub> (prostacyclin) Synthase (PTGIS, Accession NM\_000961) is another VGAM1782 host target gene. PTGIS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGIS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGIS BINDING SITE, designated SEQ ID:6669, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59584] Another function of VGAM1782 is therefore inhibition of Prostaglandin I<sub>2</sub> (prostacyclin) Synthase (PTGIS, Accession NM\_000961), a gene which catalyzes the isomerization of prostaglandin h<sub>2</sub> to prostacyclin (= prostaglandin i<sub>2</sub>). Accordingly, utilities of VGAM1782 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with PTGIS. The function of PTGIS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206.FLJ10781 (Accession NM\_018215) is another VGAM1782 host target gene. FLJ10781 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10781, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10781 BINDING SITE, designated SEQ ID:20134, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59585] Another function of VGAM1782 is therefore inhibition of FLJ10781 (Accession NM\_018215). Accordingly, utilities of VGAM1782 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10781. FLJ14397 (Accession NM\_032779) is another VGAM1782 host target gene. FLJ14397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14397, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14397 BINDING SITE, designated SEQ ID:26522, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59586] Another function of VGAM1782 is therefore inhibition of FLJ14397 (Accession NM\_032779). Accordingly, utilities of VGAM1782 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14397. KIAA1582 (Accession XM\_037262) is another VGAM1782 host target gene. KIAA1582 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1582, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1582 BINDING SITE, designated SEQ ID:32589, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59587] Another function of VGAM1782 is therefore inhibition of KIAA1582 (Accession XM\_037262). Accordingly, utilities of VGAM1782 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1582. MGC9564 (Accession NM\_080669) is another VGAM1782 host target gene. MGC9564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC9564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC9564 BINDING SITE, designated SEQ ID:27961, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59588] Another function of VGAM1782 is therefore inhibition of MGC9564 (Accession NM\_080669). Accordingly, utilities of VGAM1782 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC9564. Solute Carrier Family 26, Member 6 (SLC26A6, Accession NM\_022911) is another VGAM1782 host target gene. SLC26A6 BINDING SITE1 through SLC26A6 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC26A6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A6

BINDING SITE1 through SLC26A6 BINDING SITE3, designated SEQ ID:23217, SEQ ID:28666 and SEQ ID:28612 respectively, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59589] Another function of VGAM1782 is therefore inhibition of Solute Carrier Family 26, Member 6 (SLC26A6, Accession NM\_022911). Accordingly, utilities of VGAM1782 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A6. LOC150299 (Accession XM\_097869) is another VGAM1782 host target gene. LOC150299 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150299 BINDING SITE, designated SEQ ID:41182, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59590] Another function of VGAM1782 is therefore inhibition of LOC150299 (Accession XM\_097869). Accordingly, utilities of VGAM1782 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC150299. LOC220538 (Accession XM\_165407) is another VGAM1782 host target gene. LOC220538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220538 BINDING SITE, designated SEQ ID:43626, to the nucleotide sequence of VGAM1782 RNA, herein designated VGAM RNA, also designated SEQ ID:4493.

[59591] Another function of VGAM1782 is therefore inhibition of LOC220538 (Accession XM\_165407). Accordingly, utilities of VGAM1782 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220538. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1783 (VGAM1783) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59592] VGAM1783 is a novel bioinformatically detected regula-



tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1783 was detected is described hereinabove with reference to Figs. 1–8.

[59593] VGAM1783 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1783 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59594] VGAM1783 gene encodes a VGAM1783 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1783 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1783 precursor RNA is designated SEQ ID:1769, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1769 is located at position 33506 relative to the genome of Fowlpox Virus.

[59595] VGAM1783 precursor RNA folds onto itself, forming VGAM1783 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59596] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1783 folded precursor RNA into VGAM1783 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1783 RNA is designated SEQ ID:4494, and is provided hereinbelow with reference to the sequence listing part.

[59597] VGAM1783 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1783 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1783 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59598] VGAM1783 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1783 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1783 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1783 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1783 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59599] The complementary binding of VGAM1783 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1783 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1783 host target RNA into VGAM1783 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59600] It is appreciated that VGAM1783 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1783 host target genes. The mRNA of each one of this plurality of VGAM1783 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1783 RNA, herein designated VGAM RNA, and which when bound by VGAM1783 RNA causes inhibition of translation of respective one or more VGAM1783 host target proteins.

[59601] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1783 gene, herein designated VGAM GENE, on one or more VGAM1783 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59602] It is yet further appreciated that a function of VGAM1783 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1783 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1783 correlate with, and may be deduced from, the identity of the host target genes which VGAM1783 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59603] Nucleotide sequences of the VGAM1783 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1783 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1783 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1783 are further described hereinbelow with reference to Table 1.

[59604] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1783 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1783 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59605] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1783 gene, herein designated VGAM is inhibition of expression of VGAM1783 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1783 correlate with, and may be deduced from, the identity of the target genes which VGAM1783 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59606] Transmembrane 7 Superfamily Member 1 (upregulated in kidney) (TM7SF1, Accession NM\_003272) is a VGAM1783 host target gene. TM7SF1 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by TM7SF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TM7SF1 BINDING SITE, designated SEQ ID:9286, to the nucleotide sequence of VGAM1783 RNA, herein designated VGAM RNA, also designated SEQ ID:4494.

[59607] A function of VGAM1783 is therefore inhibition of Transmembrane 7 Superfamily Member 1 (upregulated in kidney) (TM7SF1, Accession NM\_003272). Accordingly, utilities of VGAM1783 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TM7SF1. ANKT (Accession NM\_016359) is another VGAM1783 host target gene. ANKT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKT BINDING SITE, designated SEQ ID:18499, to the nucleotide sequence of VGAM1783 RNA, herein designated VGAM RNA, also designated SEQ ID:4494.

[59608] Another function of VGAM1783 is therefore inhibition of ANKT (Accession NM\_016359). Accordingly, utilities of VGAM1783 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKT. LOC153077 (Accession XM\_098307) is another VGAM1783 host target gene. LOC153077 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153077 BINDING SITE, designated SEQ ID:41567, to the nucleotide sequence of VGAM1783 RNA, herein designated VGAM RNA, also designated SEQ ID:4494.

[59609] Another function of VGAM1783 is therefore inhibition of LOC153077 (Accession XM\_098307). Accordingly, utilities of VGAM1783 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153077. LOC91286 (Accession XM\_037444) is another VGAM1783 host target gene. LOC91286 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91286, corresponding to a HOST TARGET binding site such as BINDING



SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91286 BINDING SITE, designated SEQ ID:32620, to the nucleotide sequence of VGAM1783 RNA, herein designated VGAM RNA, also designated SEQ ID:4494.

[59610] Another function of VGAM1783 is therefore inhibition of LOC91286 (Accession XM\_037444). Accordingly, utilities of VGAM1783 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91286. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1784 (VGAM1784) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59611] VGAM1784 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1784 was detected is described hereinabove with reference to Figs. 1-8.

[59612] VGAM1784 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1784 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[59613] VGAM1784 gene encodes a VGAM1784 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1784 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1784 precursor RNA is designated SEQ ID:1770, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1770 is located at position 43278 relative to the genome of Fowlpox Virus.

[59614] VGAM1784 precursor RNA folds onto itself, forming VGAM1784 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59615] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1784 folded precursor RNA into VGAM1784

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM1784 RNA is designated SEQ ID:4495, and is provided hereinbelow with reference to the sequence listing part.

[59616] VGAM1784 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1784 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1784 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59617] VGAM1784 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1784 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1784 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1784 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1784 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59618] The complementary binding of VGAM1784 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1784 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1784 host target RNA into VGAM1784 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[59619] It is appreciated that VGAM1784 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1784 host target genes. The mRNA of each one of this plurality of VGAM1784 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1784 RNA, herein designated VGAM RNA, and which when bound by VGAM1784 RNA causes inhibition of translation of respective one or more VGAM1784 host target proteins.

[59620] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1784 gene, herein designated VGAM GENE, on one or more VGAM1784 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59621] It is yet further appreciated that a function of VGAM1784 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1784 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1784 correlate with, and may be deduced from, the identity of the host target genes which VGAM1784 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59622] Nucleotide sequences of the VGAM1784 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1784 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1784 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1784 are further described hereinbelow with reference to Table 1.

[59623] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1784 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1784 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59624] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1784 gene, herein designated VGAM is inhibition of expression of VGAM1784 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1784 correlate with, and may be deduced from, the identity of the target genes which VGAM1784 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59625] Chemokine (C-C motif) Receptor-like 1 (CCRL1, Accession NM\_016557) is a VGAM1784 host target gene. CCRL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCRL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCRL1 BINDING SITE, designated SEQ ID:18631, to the nucleotide sequence of VGAM1784 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4495.

[59626] A function of VGAM1784 is therefore inhibition of Chemokine (C-C motif) Receptor-like 1 (CCRL1, Accession NM\_016557), a gene which is a G protein-coupled receptor that binds chemokines of the CC subfamily, especially MCP-4, ELC (SCYA19) and TECK (SCYA25). Accordingly, utilities of VGAM1784 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCRL1. The function of CCRL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM546. Oxytocin Receptor (OXTR, Accession NM\_000916) is another VGAM1784 host target gene. OXTR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OXTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OXTR BINDING SITE, designated SEQ ID:6618, to the nucleotide sequence of VGAM1784 RNA, herein designated VGAM RNA, also designated SEQ ID:4495.

[59627] Another function of VGAM1784 is therefore inhibition of Oxytocin Receptor (OXTR, Accession NM\_000916), a gene



which induces inward ion currents. Accordingly, utilities of VGAM1784 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OXTR. The function of OXTR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM636.FLJ10702 (Accession NM\_018184) is another VGAM1784 host target gene. FLJ10702 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10702, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10702 BINDING SITE, designated SEQ ID:20025, to the nucleotide sequence of VGAM1784 RNA, herein designated VGAM RNA, also designated SEQ ID:4495.

[59628] Another function of VGAM1784 is therefore inhibition of FLJ10702 (Accession NM\_018184). Accordingly, utilities of VGAM1784 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10702. KIAA1013 (Accession XM\_114303) is another VGAM1784 host target gene. KIAA1013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1013 BINDING SITE, designated SEQ ID:42856, to the nucleotide sequence of VGAM1784 RNA, herein designated VGAM RNA, also designated SEQ ID:4495.

[59629] Another function of VGAM1784 is therefore inhibition of KIAA1013 (Accession XM\_114303). Accordingly, utilities of VGAM1784 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1013. SRY (sex determining region Y)-box 7 (SOX7, Accession NM\_031439) is another VGAM1784 host target gene. SOX7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOX7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX7 BINDING SITE, designated SEQ ID:25451, to the nucleotide sequence of VGAM1784 RNA, herein designated VGAM RNA, also designated SEQ ID:4495.

[59630] Another function of VGAM1784 is therefore inhibition of SRY (sex determining region Y)-box 7 (SOX7, Accession

NM\_031439). Accordingly, utilities of VGAM1784 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOX7. LOC115297 (Accession XM\_053313) is another VGAM1784 host target gene. LOC115297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115297 BINDING SITE, designated SEQ ID:36069, to the nucleotide sequence of VGAM1784 RNA, herein designated VGAM RNA, also designated SEQ ID:4495.

[59631] Another function of VGAM1784 is therefore inhibition of LOC115297 (Accession XM\_053313). Accordingly, utilities of VGAM1784 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115297. LOC221288 (Accession XM\_168058) is another VGAM1784 host target gene. LOC221288 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221288, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC221288 BINDING SITE, designated SEQ ID:44966, to the nucleotide sequence of VGAM1784 RNA, herein designated VGAM RNA, also designated SEQ ID:4495.

[59632] Another function of VGAM1784 is therefore inhibition of LOC221288 (Accession XM\_168058). Accordingly, utilities of VGAM1784 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221288. LOC90643 (Accession XM\_033145) is another VGAM1784 host target gene. LOC90643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90643 BINDING SITE, designated SEQ ID:31849, to the nucleotide sequence of VGAM1784 RNA, herein designated VGAM RNA, also designated SEQ ID:4495.

[59633] Another function of VGAM1784 is therefore inhibition of LOC90643 (Accession XM\_033145). Accordingly, utilities of VGAM1784 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90643. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1785 (VGAM1785) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59634] VGAM1785 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1785 was detected is described hereinabove with reference to Figs. 1–8.

[59635] VGAM1785 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1785 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59636] VGAM1785 gene encodes a VGAM1785 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1785 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1785 precursor RNA is designated SEQ ID:1771, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1771 is located at position 36138 relative to the genome of Fowlpox Virus.

[59637] VGAM1785 precursor RNA folds onto itself, forming VGAM1785 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59638] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1785 folded precursor RNA into VGAM1785 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1785 RNA is designated SEQ ID:4496, and is provided hereinbelow with reference to the sequence listing part.

[59639] VGAM1785 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1785 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1785 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59640] VGAM1785 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1785 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1785 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1785 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1785 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[59641] The complementary binding of VGAM1785 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1785 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1785 host target RNA into VGAM1785 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59642] It is appreciated that VGAM1785 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1785 host target genes. The mRNA of each one of this plurality of VGAM1785 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1785 RNA, herein designated VGAM RNA, and which when bound by VGAM1785 RNA causes inhibition of translation of respective one or more



VGAM1785 host target proteins.

[59643] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1785 gene, herein designated VGAM GENE, on one or more VGAM1785 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59644] It is yet further appreciated that a function of VGAM1785 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1785 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific

functions, and accordingly utilities, of VGAM1785 correlate with, and may be deduced from, the identity of the host target genes which VGAM1785 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59645] Nucleotide sequences of the VGAM1785 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1785 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1785 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1785 are further described hereinbelow with reference to Table 1.

[59646] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1785 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1785 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59647] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1785 gene, herein designated VGAM is inhibition of expression of VGAM1785 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1785 correlate with, and may be deduced from, the identity of the target genes which VGAM1785 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59648] ARP2 Actin-related Protein 2 Homolog (yeast) (ACTR2, Accession NM\_005722) is a VGAM1785 host target gene. ACTR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACTR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACTR2 BINDING SITE, designated SEQ ID:12274, to the nucleotide sequence of VGAM1785 RNA, herein designated VGAM RNA, also designated SEQ ID:4496.

[59649] A function of VGAM1785 is therefore inhibition of ARP2 Actin-related Protein 2 Homolog (yeast) (ACTR2, Accession NM\_005722). Accordingly, utilities of VGAM1785 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACTR2. FLJ20189 (Accession NM\_017704) is another VGAM1785 host target gene. FLJ20189 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by FLJ20189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20189 BINDING SITE, designated SEQ ID:19279, to the nucleotide sequence of VGAM1785 RNA, herein designated VGAM RNA, also designated SEQ ID:4496.

[59650] Another function of VGAM1785 is therefore inhibition of FLJ20189 (Accession NM\_017704). Accordingly, utilities of VGAM1785 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20189. My015 (Accession XM\_039512) is another VGAM1785 host target gene. My015 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by My015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of My015 BINDING SITE, designated SEQ ID:33107, to the nucleotide sequence of VGAM1785 RNA, herein designated VGAM RNA, also designated SEQ ID:4496.

[59651] Another function of VGAM1785 is therefore inhibition of My015 (Accession XM\_039512). Accordingly, utilities of

VGAM1785 include diagnosis, prevention and treatment of diseases and clinical conditions associated with My015. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1786 (VGAM1786) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59652] VGAM1786 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1786 was detected is described hereinabove with reference to Figs. 1–8.

[59653] VGAM1786 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1786 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59654] VGAM1786 gene encodes a VGAM1786 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1786 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1786 precursor RNA is desig-

nated SEQ ID:1772, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1772 is located at position 36018 relative to the genome of Fowlpox Virus.

- [59655] VGAM1786 precursor RNA folds onto itself, forming VGAM1786 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [59656] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1786 folded precursor RNA into VGAM1786 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM1786 RNA is designated SEQ ID:4497, and is provided hereinbelow with reference to the sequence

listing part.

[59657] VGAM1786 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1786 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1786 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59658] VGAM1786 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1786 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1786 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1786 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1786 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59659] The complementary binding of VGAM1786 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1786 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1786 host target RNA into VGAM1786 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59660] It is appreciated that VGAM1786 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1786 host target genes. The mRNA of each one of this plurality of VGAM1786 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1786 RNA, herein designated VGAM



RNA, and which when bound by VGAM1786 RNA causes inhibition of translation of respective one or more VGAM1786 host target proteins.

[59661] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1786 gene, herein designated VGAM GENE, on one or more VGAM1786 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59662] It is yet further appreciated that a function of VGAM1786 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1786 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1786 correlate with, and may be deduced from, the identity of the host target genes which VGAM1786 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59663] Nucleotide sequences of the VGAM1786 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1786 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1786 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1786 are further described hereinbelow with reference to Table 1.

[59664] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1786 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1786 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59665] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1786 gene, herein designated VGAM is

inhibition of expression of VGAM1786 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1786 correlate with, and may be deduced from, the identity of the target genes which VGAM1786 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59666] MGC16175 (Accession NM\_032765) is a VGAM1786 host target gene. MGC16175 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16175 BINDING SITE, designated SEQ ID:26513, to the nucleotide sequence of VGAM1786 RNA, herein designated VGAM RNA, also designated SEQ ID:4497.

[59667] A function of VGAM1786 is therefore inhibition of MGC16175 (Accession NM\_032765). Accordingly, utilities of VGAM1786 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16175. LOC119548 (Accession XM\_058404) is another VGAM1786 host target gene. LOC119548 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC119548, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC119548 BINDING SITE, designated SEQ ID:36617, to the nucleotide sequence of VGAM1786 RNA, herein designated VGAM RNA, also designated SEQ ID:4497.

[59668] Another function of VGAM1786 is therefore inhibition of LOC119548 (Accession XM\_058404). Accordingly, utilities of VGAM1786 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC119548. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1787 (VGAM1787) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59669] VGAM1787 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1787 was detected is described hereinabove with reference to Figs. 1-8.

[59670] VGAM1787 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Fowlpox Virus.

VGAM1787 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59671] VGAM1787 gene encodes a VGAM1787 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1787 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1787 precursor RNA is designated SEQ ID:1773, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1773 is located at position 44889 relative to the genome of Fowlpox Virus.

[59672] VGAM1787 precursor RNA folds onto itself, forming VGAM1787 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59673] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1787 folded precursor RNA into VGAM1787 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1787 RNA is designated SEQ ID:4498, and is provided hereinbelow with reference to the sequence listing part.

[59674] VGAM1787 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1787 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1787 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59675] VGAM1787 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1787 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1787 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1787 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1787 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59676] The complementary binding of VGAM1787 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1787 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1787

host target RNA into VGAM1787 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59677] It is appreciated that VGAM1787 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1787 host target genes. The mRNA of each one of this plurality of VGAM1787 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1787 RNA, herein designated VGAM RNA, and which when bound by VGAM1787 RNA causes inhibition of translation of respective one or more VGAM1787 host target proteins.

[59678] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1787 gene, herein designated VGAM GENE, on one or more VGAM1787 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59679] It is yet further appreciated that a function of VGAM1787 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1787 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1787 correlate with, and may be deduced from, the identity of the host target genes which VGAM1787 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59680] Nucleotide sequences of the VGAM1787 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1787 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1787 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1787 are further

described hereinbelow with reference to Table 1.

[59681] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1787 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1787 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59682] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1787 gene, herein designated VGAM is inhibition of expression of VGAM1787 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1787 correlate with, and may be deduced from, the identity of the target genes which VGAM1787 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59683] BLAME (Accession NM\_020125) is a VGAM1787 host target gene. BLAME BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BLAME, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLAME BINDING SITE, designated SEQ

ID:21304, to the nucleotide sequence of VGAM1787 RNA, herein designated VGAM RNA, also designated SEQ ID:4498.

[59684] A function of VGAM1787 is therefore inhibition of BLAME (Accession NM\_020125). Accordingly, utilities of VGAM1787 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLAME. RNA Binding Motif Protein 3 (RBM3, Accession XM\_047024) is another VGAM1787 host target gene. RBM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RBM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBM3 BINDING SITE, designated SEQ ID:34895, to the nucleotide sequence of VGAM1787 RNA, herein designated VGAM RNA, also designated SEQ ID:4498.

[59685] Another function of VGAM1787 is therefore inhibition of RNA Binding Motif Protein 3 (RBM3, Accession XM\_047024). Accordingly, utilities of VGAM1787 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBM3. LOC152002 (Accession XM\_087360) is another VGAM1787 host target

gene. LOC152002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152002 BINDING SITE, designated SEQ ID:39193, to the nucleotide sequence of VGAM1787 RNA, herein designated VGAM RNA, also designated SEQ ID:4498.

[59686] Another function of VGAM1787 is therefore inhibition of LOC152002 (Accession XM\_087360). Accordingly, utilities of VGAM1787 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152002. LOC92979 (Accession NM\_138396) is another VGAM1787 host target gene. LOC92979 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92979 BINDING SITE, designated SEQ ID:28763, to the nucleotide sequence of VGAM1787 RNA, herein designated VGAM RNA, also designated SEQ ID:4498.

[59687] Another function of VGAM1787 is therefore inhibition of LOC92979 (Accession NM\_138396). Accordingly, utilities of VGAM1787 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92979. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1788 (VGAM1788) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59688] VGAM1788 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1788 was detected is described hereinabove with reference to Figs. 1–8.

[59689] VGAM1788 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1788 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59690] VGAM1788 gene encodes a VGAM1788 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1788 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1788 precursor RNA is designated SEQ ID:1774, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1774 is located at position 45071 relative to the genome of Fowlpox Virus.

[59691] VGAM1788 precursor RNA folds onto itself, forming VGAM1788 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59692] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1788 folded precursor RNA into VGAM1788 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1788 RNA is designated SEQ ID:4499, and is provided hereinbelow with reference to the sequence listing part.

[59693] VGAM1788 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1788 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1788 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[59694] VGAM1788 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1788 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1788 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1788 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1788 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59695] The complementary binding of VGAM1788 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1788 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1788 host target RNA into VGAM1788 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59696] It is appreciated that VGAM1788 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1788 host target genes. The mRNA of each one of this plurality of VGAM1788 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1788 RNA, herein designated VGAM RNA, and which when bound by VGAM1788 RNA causes inhibition of translation of respective one or more VGAM1788 host target proteins.

[59697] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1788 gene, herein designated VGAM GENE, on one or more VGAM1788 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59698] It is yet further appreciated that a function of VGAM1788 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1788 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1788 correlate with, and may be deduced from, the identity of the host target genes which VGAM1788 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59699] Nucleotide sequences of the VGAM1788 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1788 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1788 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1788 are further described hereinbelow with reference to Table 1.

[59700] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1788 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1788 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[59701] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1788 gene, herein designated VGAM is inhibition of expression of VGAM1788 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1788 correlate with, and may be deduced from, the identity of the target genes which VGAM1788 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59702] CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM\_054838) is a VGAM1788 host target gene. CSMD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSMD1 BINDING SITE, designated SEQ ID:36196, to the nucleotide sequence of VGAM1788 RNA, herein designated VGAM RNA, also designated SEQ ID:4499.

[59703] A function of VGAM1788 is therefore inhibition of CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM\_054838). Accordingly, utilities of VGAM1788 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with CSMD1. PRO2389 (Accession XM\_033334) is another VGAM1788 host target gene. PRO2389 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO2389, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2389 BINDING SITE, designated SEQ ID:31881, to the nucleotide sequence of VGAM1788 RNA, herein designated VGAM RNA, also designated SEQ ID:4499.

[59704] Another function of VGAM1788 is therefore inhibition of PRO2389 (Accession XM\_033334). Accordingly, utilities of VGAM1788 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2389. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1789 (VGAM1789) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59705] VGAM1789 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1789 was detected is described hereinabove with reference to Figs. 1–8.

[59706] VGAM1789 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1789 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59707] VGAM1789 gene encodes a VGAM1789 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1789 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1789 precursor RNA is designated SEQ ID:1775, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1775 is located at position 42299 relative to the genome of Fowlpox Virus.

[59708] VGAM1789 precursor RNA folds onto itself, forming VGAM1789 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59709] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1789 folded precursor RNA into VGAM1789 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1789 RNA is designated SEQ ID:4500, and is provided hereinbelow with reference to the sequence listing part.

[59710] VGAM1789 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1789 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1789 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59711] VGAM1789 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1789 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1789 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1789 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1789 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59712] The complementary binding of VGAM1789 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1789 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1789 host target RNA into VGAM1789 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59713] It is appreciated that VGAM1789 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1789 host target genes. The mRNA of each one of this plurality of VGAM1789 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1789 RNA, herein designated VGAM RNA, and which when bound by VGAM1789 RNA causes inhibition of translation of respective one or more VGAM1789 host target proteins.

[59714] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1789 gene, herein designated VGAM GENE, on one or more VGAM1789 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59715] It is yet further appreciated that a function of VGAM1789 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1789 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1789 correlate with, and may be deduced from, the identity of the host target genes which VGAM1789 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59716] Nucleotide sequences of the VGAM1789 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1789 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1789 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1789 are further described hereinbelow with reference to Table 1.

[59717] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1789 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1789 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59718] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1789 gene, herein designated VGAM is inhibition of expression of VGAM1789 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1789 correlate with, and may be deduced from, the identity of the target genes which VGAM1789 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59719] Norrie Disease (pseudoglioma) (NDP, Accession NM\_000266) is a VGAM1789 host target gene. NDP BINDING SITE is HOST TARGET binding site found in the 3` un-

translated region of mRNA encoded by NDP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDP BINDING SITE, designated SEQ ID:5807, to the nucleotide sequence of VGAM1789 RNA, herein designated VGAM RNA, also designated SEQ ID:4500.

[59720] A function of VGAM1789 is therefore inhibition of Norrie Disease (pseudoglioma) (NDP, Accession NM\_000266), a gene which may be involved in a pathway that regulates neural cell differentiation and proliferation. Accordingly, utilities of VGAM1789 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDP. The function of NDP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM113.DKFZp761F2014 (Accession NM\_020215) is another VGAM1789 host target gene. DKFZp761F2014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761F2014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of DKFZp761F2014 BINDING SITE, designated SEQ ID:21463, to the nucleotide sequence of VGAM1789 RNA, herein designated VGAM RNA, also designated SEQ ID:4500.

[59721] Another function of VGAM1789 is therefore inhibition of DKFZp761F2014 (Accession NM\_020215). Accordingly, utilities of VGAM1789 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761F2014. FLJ23590 (Accession NM\_024649) is another VGAM1789 host target gene. FLJ23590 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23590, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23590 BINDING SITE, designated SEQ ID:23941, to the nucleotide sequence of VGAM1789 RNA, herein designated VGAM RNA, also designated SEQ ID:4500.

[59722] Another function of VGAM1789 is therefore inhibition of FLJ23590 (Accession NM\_024649). Accordingly, utilities of VGAM1789 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23590. KIAA0016 (Accession NM\_014765) is another

VGAM1789 host target gene. KIAA0016 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0016 BINDING SITE, designated SEQ ID:16535, to the nucleotide sequence of VGAM1789 RNA, herein designated VGAM RNA, also designated SEQ ID:4500.

[59723] Another function of VGAM1789 is therefore inhibition of KIAA0016 (Accession NM\_014765). Accordingly, utilities of VGAM1789 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0016. LOC145566 (Accession XM\_085174) is another VGAM1789 host target gene. LOC145566 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145566 BINDING SITE, designated SEQ ID:37901, to the nucleotide sequence of VGAM1789 RNA, herein designated VGAM RNA, also designated SEQ ID:4500.

[59724] Another function of VGAM1789 is therefore inhibition of LOC145566 (Accession XM\_085174). Accordingly, utilities of VGAM1789 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145566. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1790 (VGAM1790) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59725] VGAM1790 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1790 was detected is described hereinabove with reference to Figs. 1–8.

[59726] VGAM1790 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1790 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59727] VGAM1790 gene encodes a VGAM1790 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1790 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1790 precursor RNA is designated SEQ ID:1776, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1776 is located at position 79077 relative to the genome of Rana Tigrina Ranavirus.

[59728] VGAM1790 precursor RNA folds onto itself, forming VGAM1790 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59729] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1790 folded precursor RNA into VGAM1790 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1790 RNA is designated SEQ ID:4501, and is provided hereinbelow with reference to the sequence listing part.

[59730] VGAM1790 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1790 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1790 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[59731] VGAM1790 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1790 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1790 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the



number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1790 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1790 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59732] The complementary binding of VGAM1790 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1790 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1790 host target RNA into VGAM1790 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59733] It is appreciated that VGAM1790 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1790 host target genes. The mRNA of each one of this plurality of VGAM1790 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1790 RNA, herein designated VGAM RNA, and which when bound by VGAM1790 RNA causes inhibition of translation of respective one or more VGAM1790 host target proteins.

[59734] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1790 gene, herein designated VGAM GENE, on one or more VGAM1790 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59735] It is yet further appreciated that a function of VGAM1790 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1790 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1790 correlate with, and may be deduced from, the identity of the host target genes which VGAM1790 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59736] Nucleotide sequences of the VGAM1790 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1790 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1790 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1790 are further described hereinbelow with reference to Table 1.

[59737] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1790 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1790 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[59738] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1790 gene, herein designated VGAM is inhibition of expression of VGAM1790 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1790 correlate with, and may be deduced from, the identity of the target genes which VGAM1790 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59739] Peroxisome Proliferative Activated Receptor, Gamma, Coactivator 1 (PPARGC1, Accession NM\_013261) is a VGAM1790 host target gene. PPARGC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPARGC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPARGC1 BINDING SITE, designated SEQ ID:14931, to the nucleotide sequence of VGAM1790 RNA, herein designated VGAM RNA, also designated SEQ ID:4501.

[59740] A function of VGAM1790 is therefore inhibition of Peroxisome Proliferative Activated Receptor, Gamma, Coactivator 1 (PPARGC1, Accession NM\_013261), a gene which

may play a role in insulin sensitivity and thermogenesis. Accordingly, utilities of VGAM1790 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPARGC1. The function of PPARGC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM952. PRO1575 (Accession NM\_014092) is another VGAM1790 host target gene. PRO1575 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1575, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1575 BINDING SITE, designated SEQ ID:15312, to the nucleotide sequence of VGAM1790 RNA, herein designated VGAM RNA, also designated SEQ ID:4501.

[59741] Another function of VGAM1790 is therefore inhibition of PRO1575 (Accession NM\_014092). Accordingly, utilities of VGAM1790 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1575. LOC90141 (Accession XM\_029373) is another VGAM1790 host target gene. LOC90141 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90141, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90141 BINDING SITE, designated SEQ ID:30881, to the nucleotide sequence of VGAM1790 RNA, herein designated VGAM RNA, also designated SEQ ID:4501.

[59742] Another function of VGAM1790 is therefore inhibition of LOC90141 (Accession XM\_029373). Accordingly, utilities of VGAM1790 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90141. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1791 (VGAM1791) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59743] VGAM1791 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1791 was detected is described hereinabove with reference to Figs. 1-8.

[59744] VGAM1791 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1791 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59745] VGAM1791 gene encodes a VGAM1791 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1791 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1791 precursor RNA is designated SEQ ID:1777, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1777 is located at position 85010 relative to the genome of Rana Tigrina Ranavirus.

[59746] VGAM1791 precursor RNA folds onto itself, forming VGAM1791 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[59747] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1791 folded precursor RNA into VGAM1791 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1791 RNA is designated SEQ ID:4502, and is provided hereinbelow with reference to the sequence listing part.

[59748] VGAM1791 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1791 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1791 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59749] VGAM1791 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1791 host target



RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1791 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1791 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1791 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59750] The complementary binding of VGAM1791 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1791 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1791 host target RNA into VGAM1791 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59751] It is appreciated that VGAM1791 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1791 host target genes. The mRNA of each one of this plurality of VGAM1791 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1791 RNA, herein designated VGAM RNA, and which when bound by VGAM1791 RNA causes inhibition of translation of respective one or more VGAM1791 host target proteins.

[59752] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1791 gene, herein designated VGAM GENE, on one or more VGAM1791 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59753] It is yet further appreciated that a function of VGAM1791 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1791 correlate with, and may be deduced from, the identity of the host target genes which VGAM1791 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59754] Nucleotide sequences of the VGAM1791 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1791 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1791 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1791 are further described hereinbelow with reference to Table 1.

[59755] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1791 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1791 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59756] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1791 gene, herein designated VGAM is inhibition of expression of VGAM1791 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1791 correlate with, and may be deduced from, the identity of the target genes which VGAM1791 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59757] UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM\_033171) is a VGAM1791 host target gene. B3GALT5 BINDING SITE1 through B3GALT5 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GALT5, corresponding to HOST TARGET binding

sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT5 BINDING SITE1 through B3GALT5 BINDING SITE4, designated SEQ ID:27026, SEQ ID:27036, SEQ ID:27031 and SEQ ID:12698 respectively, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59758] A function of VGAM1791 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM\_033171). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT5. Gap Junction Protein, Beta 3, 31kDa (connexin 31) (GJB3, Accession NM\_024009) is another VGAM1791 host target gene. GJB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GJB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GJB3 BINDING SITE, designated SEQ ID:23437, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59759] Another function of VGAM1791 is therefore inhibition of Gap Junction Protein, Beta 3, 31kDa (connexin 31) (GJB3, Accession NM\_024009). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GJB3. Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM\_085943) is another VGAM1791 host target gene. GRLF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRLF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRLF1 BINDING SITE, designated SEQ ID:38408, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59760] Another function of VGAM1791 is therefore inhibition of Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM\_085943), a gene which inhibits transcription of the glucocorticoid receptor gene. Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRLF1. The function of GRLF1 and its association with

various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.MAX Binding Protein (MNT, Accession NM\_020310) is another VGAM1791 host target gene. MNT BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MNT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MNT BINDING SITE, designated SEQ ID:21565, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59761] Another function of VGAM1791 is therefore inhibition of MAX Binding Protein (MNT, Accession NM\_020310). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MNT. Metastasis-associated 1-like 1 (MTA1L1, Accession NM\_004739) is another VGAM1791 host target gene. MTA1L1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MTA1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of MTA1L1 BINDING SITE, designated SEQ ID:11136, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59762] Another function of VGAM1791 is therefore inhibition of Metastasis-associated 1-like 1 (MTA1L1, Accession NM\_004739), a gene which regulates histone deacetylase core complex enzymatic activity. Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTA1L1. The function of MTA1L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM659. Promyelocytic Leukemia (PML, Accession NM\_033240) is another VGAM1791 host target gene. PML BINDING SITE1 and PML BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PML, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PML BINDING SITE1 and PML BINDING SITE2, designated SEQ ID:27079 and SEQ ID:27083 respectively, to the nucleotide sequence of



VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59763] Another function of VGAM1791 is therefore inhibition of Promyelocytic Leukemia (PML, Accession NM\_033240). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PML. Chromosome 20 Open Reading Frame 112 (C20orf112, Accession NM\_080616) is another VGAM1791 host target gene. C20orf112 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf112 BINDING SITE, designated SEQ ID:27931, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59764] Another function of VGAM1791 is therefore inhibition of Chromosome 20 Open Reading Frame 112 (C20orf112, Accession NM\_080616). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf112. FLJ12488 (Accession NM\_031218) is another

VGAM1791 host target gene. FLJ12488 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12488, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12488 BINDING SITE, designated SEQ ID:25264, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59765] Another function of VGAM1791 is therefore inhibition of FLJ12488 (Accession NM\_031218). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12488. FLJ23392 (Accession NM\_024784) is another VGAM1791 host target gene. FLJ23392 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23392, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23392 BINDING SITE, designated SEQ ID:24159, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59766] Another function of VGAM1791 is therefore inhibition of FLJ23392 (Accession NM\_024784). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23392. KIAA0153 (Accession NM\_015140) is another VGAM1791 host target gene. KIAA0153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0153 BINDING SITE, designated SEQ ID:17495, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59767] Another function of VGAM1791 is therefore inhibition of KIAA0153 (Accession NM\_015140). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0153. KIAA0555 (Accession NM\_014790) is another VGAM1791 host target gene. KIAA0555 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0555, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0555 BINDING SITE, designated SEQ ID:16678, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59768] Another function of VGAM1791 is therefore inhibition of KIAA0555 (Accession NM\_014790). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0555. KIAA1204 (Accession XM\_045011) is another VGAM1791 host target gene. KIAA1204 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1204, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1204 BINDING SITE, designated SEQ ID:34313, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59769] Another function of VGAM1791 is therefore inhibition of KIAA1204 (Accession XM\_045011). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1204. KIAA1755 (Accession XM\_028810) is another VGAM1791 host target gene. KIAA1755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1755, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1755 BINDING SITE, designated SEQ ID:30746, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59770] Another function of VGAM1791 is therefore inhibition of KIAA1755 (Accession XM\_028810). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1755. KIAA1908 (Accession XM\_055834) is another VGAM1791 host target gene. KIAA1908 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1908 BINDING SITE, designated SEQ ID:36330, to the nucleotide sequence of VGAM1791 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4502.

[59771] Another function of VGAM1791 is therefore inhibition of KIAA1908 (Accession XM\_055834). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1908. Myosin, Heavy Polypeptide 10, Non-muscle (MYH10, Accession XM\_044702) is another VGAM1791 host target gene. MYH10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYH10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYH10 BINDING SITE, designated SEQ ID:34264, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59772] Another function of VGAM1791 is therefore inhibition of Myosin, Heavy Polypeptide 10, Non-muscle (MYH10, Accession XM\_044702). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYH10. TOLLIP (Accession NM\_019009) is another VGAM1791 host target gene. TOLLIP BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by TOLLIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOLLIP BINDING SITE, designated SEQ ID:21090, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59773] Another function of VGAM1791 is therefore inhibition of TOLLIP (Accession NM\_019009). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOLLIP. LOC143451 (Accession XM\_084521) is another VGAM1791 host target gene. LOC143451 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143451 BINDING SITE, designated SEQ ID:37620, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59774] Another function of VGAM1791 is therefore inhibition of

LOC143451 (Accession XM\_084521). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143451. LOC145125 (Accession XM\_085025) is another VGAM1791 host target gene. LOC145125 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145125, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145125 BINDING SITE, designated SEQ ID:37797, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59775] Another function of VGAM1791 is therefore inhibition of LOC145125 (Accession XM\_085025). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145125. LOC147495 (Accession XM\_097240) is another VGAM1791 host target gene. LOC147495 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC147495 BINDING SITE, designated SEQ ID:40839, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59776] Another function of VGAM1791 is therefore inhibition of LOC147495 (Accession XM\_097240). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147495. LOC158158 (Accession XM\_088494) is another VGAM1791 host target gene. LOC158158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158158 BINDING SITE, designated SEQ ID:39733, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59777] Another function of VGAM1791 is therefore inhibition of LOC158158 (Accession XM\_088494). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158158. LOC254440 (Accession XM\_173126) is an-

other VGAM1791 host target gene. LOC254440 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254440, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254440 BINDING SITE, designated SEQ ID:46374, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59778] Another function of VGAM1791 is therefore inhibition of LOC254440 (Accession XM\_173126). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254440. LOC256310 (Accession XM\_172813) is another VGAM1791 host target gene. LOC256310 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256310 BINDING SITE, designated SEQ ID:46092, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59779] Another function of VGAM1791 is therefore inhibition of LOC256310 (Accession XM\_172813). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256310. LOC93356 (Accession XM\_050744) is another VGAM1791 host target gene. LOC93356 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC93356, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93356 BINDING SITE, designated SEQ ID:35671, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59780] Another function of VGAM1791 is therefore inhibition of LOC93356 (Accession XM\_050744). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93356. LOC93496 (Accession XM\_051698) is another VGAM1791 host target gene. LOC93496 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC93496, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93496 BINDING SITE, designated SEQ ID:35865, to the nucleotide sequence of VGAM1791 RNA, herein designated VGAM RNA, also designated SEQ ID:4502.

[59781] Another function of VGAM1791 is therefore inhibition of LOC93496 (Accession XM\_051698). Accordingly, utilities of VGAM1791 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93496. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1792 (VGAM1792) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59782] VGAM1792 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1792 was detected is described hereinabove with reference to Figs. 1-8.

[59783] VGAM1792 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1792 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[59784] VGAM1792 gene encodes a VGAM1792 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1792 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1792 precursor RNA is designated SEQ ID:1778, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1778 is located at position 75405 relative to the genome of Rana Tigrina Ranavirus.

[59785] VGAM1792 precursor RNA folds onto itself, forming VGAM1792 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59786] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1792 folded precursor RNA into VGAM1792

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM1792 RNA is designated SEQ ID:4503, and is provided hereinbelow with reference to the sequence listing part.

[59787] VGAM1792 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1792 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1792 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59788] VGAM1792 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1792 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1792 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1792 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1792 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59789] The complementary binding of VGAM1792 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1792 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1792 host target RNA into VGAM1792 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[59790] It is appreciated that VGAM1792 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1792 host target genes. The mRNA of each one of this plurality of VGAM1792 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1792 RNA, herein designated VGAM RNA, and which when bound by VGAM1792 RNA causes inhibition of translation of respective one or more VGAM1792 host target proteins.

[59791] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1792 gene, herein designated VGAM GENE, on one or more VGAM1792 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59792] It is yet further appreciated that a function of VGAM1792 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1792 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1792 correlate with, and may be deduced from, the identity of the host target genes which VGAM1792 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59793] Nucleotide sequences of the VGAM1792 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1792 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1792 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1792 are further described hereinbelow with reference to Table 1.

[59794] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1792 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1792 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59795] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1792 gene, herein designated VGAM is inhibition of expression of VGAM1792 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1792 correlate with, and may be deduced from, the identity of the target genes which VGAM1792 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59796] Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11, Accession NM\_002474) is a VGAM1792 host target gene. MYH11 BINDING SITE1 and MYH11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MYH11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYH11 BINDING SITE1 and MYH11 BINDING SITE2, designated SEQ ID:8300

and SEQ ID:23142 respectively, to the nucleotide sequence of VGAM1792 RNA, herein designated VGAM RNA, also designated SEQ ID:4503.

[59797] A function of VGAM1792 is therefore inhibition of Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11, Accession NM\_002474), a gene which is involved in muscle contraction. Accordingly, utilities of VGAM1792 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYH11. The function of MYH11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Calcium/calmodulin-dependent Protein Kinase Kinase 2, Beta (CAMKK2, Accession NM\_006549) is another VGAM1792 host target gene. CAMKK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK2 BINDING SITE, designated SEQ ID:13316, to the nucleotide sequence of VGAM1792 RNA, herein designated VGAM RNA, also designated SEQ ID:4503.

[59798] Another function of VGAM1792 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 2, Beta (CAMKK2, Accession NM\_006549). Accordingly, utilities of VGAM1792 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK2. FLJ32894 (Accession NM\_144667) is another VGAM1792 host target gene. FLJ32894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32894 BINDING SITE, designated SEQ ID:29485, to the nucleotide sequence of VGAM1792 RNA, herein designated VGAM RNA, also designated SEQ ID:4503.

[59799] Another function of VGAM1792 is therefore inhibition of FLJ32894 (Accession NM\_144667). Accordingly, utilities of VGAM1792 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32894. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1793 (VGAM1793) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59800] VGAM1793 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1793 was detected is described hereinabove with reference to Figs. 1–8.

[59801] VGAM1793 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1793 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59802] VGAM1793 gene encodes a VGAM1793 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1793 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1793 precursor RNA is designated SEQ ID:1779, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1779 is located at position 85120 relative to the genome of Rana Tigrina Ranavirus.

[59803] VGAM1793 precursor RNA folds onto itself, forming

VGAM1793 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59804] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1793 folded precursor RNA into VGAM1793 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1793 RNA is designated SEQ ID:4504, and is provided hereinbelow with reference to the sequence listing part.

[59805] VGAM1793 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1793 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1793 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59806] VGAM1793 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1793 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1793 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1793 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1793 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59807] The complementary binding of VGAM1793 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1793 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1793 host target RNA into VGAM1793 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59808] It is appreciated that VGAM1793 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1793 host target genes. The mRNA of each one of this plurality of VGAM1793 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1793 RNA, herein designated VGAM RNA, and which when bound by VGAM1793 RNA causes inhibition of translation of respective one or more VGAM1793 host target proteins.

[59809] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with



specific reference to translational inhibition exerted by VGAM1793 gene, herein designated VGAM GENE, on one or more VGAM1793 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59810] It is yet further appreciated that a function of VGAM1793 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1793 correlate with, and may be deduced from, the identity of the host target genes which VGAM1793 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[59811] Nucleotide sequences of the VGAM1793 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1793 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1793 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1793 are further described hereinbelow with reference to Table 1.

[59812] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1793 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1793 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59813] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1793 gene, herein designated VGAM is inhibition of expression of VGAM1793 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1793 correlate with, and may be deduced from, the identity of the target genes which VGAM1793 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[59814] Amphiregulin (schwannoma-derived growth factor) (AREG, Accession NM\_001657) is a VGAM1793 host target gene. AREG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AREG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AREG BINDING SITE, designated SEQ ID:7376, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59815] A function of VGAM1793 is therefore inhibition of Amphiregulin (schwannoma-derived growth factor) (AREG, Accession NM\_001657), a gene which inhibits the growth of certain carcinoma cell lines but stimulates the growth of fibroblasts and epithelial cells. Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AREG. The function of AREG has been established by previous studies. To identify new growth factors important to the development of the nervous system, Kimura et al. (1990) screened serum-free growth-conditioned media from many clonal cell lines for the presence of mitogens for

CNS glial cells. A cell line secreting a potent glial mitogen was established from a schwannoma of the sciatic nerve. The cells of the tumor, named JS1 cells, were adapted to clonal culture and identified as Schwann cells. Schwann cells secrete an autocrine mitogen and human schwannoma extracts have mitogenic activity on glial cells.

Kimura et al. (1990) reported the purification and characterization of the mitogenic molecule, designated schwannoma-derived growth factor (SDGF), from the growth-conditioned medium of the JS1 Schwann cell line. SDGF belongs to the epidermal growth factor family and is an autocrine growth factor as well as a mitogen for astrocytes, Schwann cells, and fibroblasts. Amphiregulin is a heparin-binding, heparin-inhibited member of the epidermal growth factor family and an autocrine growth factor for human keratinocytes. AREG expression is increased in psoriatic epidermis. To test the hypothesis that aberrant AREG expression is central to the development of psoriatic lesions, Cook et al. (1997) constructed a transgene encoding the human AREG gene driven by the promoter of human keratin 14 (OMIM Ref. No. 148066). They found that transgene integration and subsequent expression of AREG in basal keratinocytes correlated with a pso-

riasis-like skin phenotype. Afflicted mice demonstrated shortened life spans, prominent scaling and erythematous skin with alopecia, and occasional papillomatous epidermal growths. Histologic examination revealed extensive areas of marked hyperkeratosis with focal parakeratosis, acanthosis, dermal and epidermal lymphocytic and neutrophilic infiltration, and dilated blood vessels within the papillary dermis. The skin pathology was considered to be strikingly similar to psoriasis. The observations of Cook et al. (1997) linked the keratinocyte EGF receptor-ligand system to psoriatic inflammation and suggested that aberrant expression of AREG in the epidermis may represent a critical step in the development or propagation of psoriatic lesions.

[59816] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59817] Cook, P. W.; Piepkorn, M.; Clegg, C. H.; Plowman, G. D.; DeMay, J. M.; Brown, J. R.; Pittelkow, M. R. : Transgenic expression of the human amphiregulin gene induces a psoriasis-like phenotype. J. Clin. Invest. 100: 2286-2294, 1997. ; and

[59818] Kimura, H.; Fischer, W. H.; Schubert, D. : Structure, ex-

pression and function of a schwannoma-derived growth factor. Nature 348: 257-260, 1990.

[59819] Further studies establishing the function and utilities of AREG are found in John Hopkins OMIM database record ID 104640, and in cited publications numbered 12266-12268, 26 and 12414-12415 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rho GTPase Activating Protein 6 (ARHGAP6, Accession NM\_001174) is another VGAM1793 host target gene. ARHGAP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARHGAP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP6 BINDING SITE, designated SEQ ID:6843, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59820] Another function of VGAM1793 is therefore inhibition of Rho GTPase Activating Protein 6 (ARHGAP6, Accession NM\_001174), a gene which activates the rho-type GTPases by converting them to an inactive GTP-bound state. Accordingly, utilities of VGAM1793 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with ARHGAP6. The function of ARHGAP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM55.Calmodulin 3 (phosphorylase kinase, delta) (CALM3, Accession NM\_005184) is another VGAM1793 host target gene. CALM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALM3 BINDING SITE, designated SEQ ID:11684, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59821] Another function of VGAM1793 is therefore inhibition of Calmodulin 3 (phosphorylase kinase, delta) (CALM3, Accession NM\_005184), a gene which mediates the control of a large number of enzymes by  $Ca^{++}$ . Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALM3. The function of CALM3 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM785. DnaJ (Hsp40) Homolog, Subfamily B, Member 9 (DNAJB9, Accession NM\_012328) is another VGAM1793 host target gene. DNAJB9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DNAJB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJB9 BINDING SITE, designated SEQ ID:14718, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59822] Another function of VGAM1793 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily B, Member 9 (DNAJB9, Accession NM\_012328). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJB9. EphA8 (EPHA8, Accession NM\_020526) is another VGAM1793 host target gene. EPHA8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE



II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA8 BINDING SITE, designated SEQ ID:21746, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59823] Another function of VGAM1793 is therefore inhibition of EphA8 (EPHA8, Accession NM\_020526), a gene which Eph-related receptor tyrosine kinase A8. Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA8. The function of EPHA8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM494. Ellis Van Creveld Syndrome (EVC, Accession NM\_014556) is another VGAM1793 host target gene. EVC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EVC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVC BINDING SITE, designated SEQ ID:15882, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ

ID:4504.

[59824] Another function of VGAM1793 is therefore inhibition of Ellis Van Creveld Syndrome (EVC, Accession NM\_014556). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVC. Guanine Nucleotide Binding Protein (G protein), Alpha 15 (Gq class) (GNA15, Accession XM\_009220) is another VGAM1793 host target gene. GNA15 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GNA15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNA15 BINDING SITE, designated SEQ ID:30103, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59825] Another function of VGAM1793 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha 15 (Gq class) (GNA15, Accession XM\_009220). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNA15. 5-hydroxytryptamine (serotonin) Receptor

1D (HTR1D, Accession NM\_000864) is another VGAM1793 host target gene. HTR1D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTR1D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR1D BINDING SITE, designated SEQ ID:6530, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59826] Another function of VGAM1793 is therefore inhibition of 5-hydroxytryptamine (serotonin) Receptor 1D (HTR1D, Accession NM\_000864), a gene which belongs to G-protein coupled receptor. Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR1D. The function of HTR1D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Immediate Early Response 3 (IER3, Accession NM\_003897) is another VGAM1793 host target gene. IER3 BINDING SITE1 and IER3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA en-

coded by IER3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IER3 BINDING SITE1 and IER3 BINDING SITE2, designated SEQ ID:9980 and SEQ ID:27400 respectively, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59827] Another function of VGAM1793 is therefore inhibition of Immediate Early Response 3 (IER3, Accession NM\_003897), a gene which protects cells from apoptosis induced by FAS or TNFA. Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IER3. The function of IER3 has been established by previous studies. Transcription factors of the nuclear factor-kappa-B/rel (NF-kappa-B) family (OMIM Ref. No. 164011) may be important in cell survival by regulating unidentified, anti-apoptotic genes. Charles et al. (1993) cloned gly96, a mouse immediate-early gene inducible by serum growth factors. Schafer et al. (1996) cloned the rat homolog, PRG1, which was induced in response to the pituitary adenylate cyclase-activating polypeptide (PACAP;

102980). Kondratyev et al. (1996) cloned the human immediate-early gene IEX1. The cDNA encodes 156-amino acid polypeptide containing a single predicted transmembrane domain. On Northern blots, they observed a 1.2-kb mRNA whose expression could be induced by ionizing radiation, 12-O-tetradecanoylphorbol-13-acetate (TPA), okadaic acid, and TNF-alpha (OMIM Ref. No. 191160); these agents are all activators of the protein kinase C (PKC; OMIM Ref. No. 176960) pathway. Pietzsch et al. (1997) cloned the same human gene, which they termed DIF2. The expression of the DIF2 mRNA is downregulated during differentiation of macrophages and upregulated by lipopolysaccharide (LPS) stimulation of monocytes. Northern blot analysis revealed that DIF2 is expressed most abundantly in monocytes, lymphocytes, and keratinocytes, and at a lesser level in several other human tissues and cell lines. Wu et al. (1998) described a gene that protects cells from apoptosis induced by FAS (OMIM Ref. No. 134637) or TNFA. The gene appeared to be the same as the immediate-early response gene IEX1 reported by Kondratyev et al. (1996), Charles et al. (1993), and Schafer et al. (1996), except that it had an in-frame insertion of 111 nucleotides at position 211 of the coding region of IEX1,

and could encode a longer polypeptide with a 37-amino acid insertion relative to IEX1. The longer IEX1 (referred to as IEX1L; the original IEX1 was referred to as IEX1S) was found to be generated from IEX1 in the absence of RNA splicing as it contained the entire intron sequence of IEX1. The transcription of IEX1L induced by TNF was decreased in cells with defective NF-kappa-B activation, rendering them sensitive to TNF-induced apoptosis, which was abolished by transfection with IEX1L. In support, overexpression of antisense IEX1L partially blocked TNF-induced expression of IEX1L and sensitized normal cells to killing. This study demonstrated a key role of IEX1L in cellular resistance to TNF-induced apoptosis. Pietzsch et al. (1998) cloned the genomic DNA of the DIF2 gene. They found that the gene consists of 2 exons and a single small intron. The 5-prime flanking region of the gene contains binding sites for transcription factors including NF-kappa-B, CEBP (OMIM Ref. No. 116897), and SP1 (OMIM Ref. No. 189906). Pietzsch et al. (1998) used fluorescence in situ hybridization to map the IER3 gene to human chromosome 6p21.3.

[59828] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [59829] Pietzsch, A.; Buchler, C.; Schmitz, G. : Genomic organization, promoter cloning, and chromosomal localization of the Dif-2 gene. *Biochem. Biophys. Res. Commun.* 245: 651-657, 1998. ; and
- [59830] Wu, M. X.; Ao, Z.; Prasad, K. V. S.; Wu, R.; Schlossman, S. F. : IEX-1L, an apoptosis inhibitor involved in NF-kappa-B-mediated cell survival. *Science* 281: 998-1001, 1998.
- [59831] Further studies establishing the function and utilities of IER3 are found in John Hopkins OMIM database record ID 602996, and in cited publications numbered 5412-5417 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mucin 3B (MUC3B, Accession XM\_168578) is another VGAM1793 host target gene. MUC3B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MUC3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC3B BINDING SITE, designated SEQ ID:45253, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ

ID:4504.

[59832] Another function of VGAM1793 is therefore inhibition of Mucin 3B (MUC3B, Accession XM\_168578), a gene which provides a protective, lubricating barrier against particles and infectious agents at mucosal surfaces. Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC3B. The function of MUC3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Myosin Light Chain Kinase 2, Skeletal Muscle (MYLK2, Accession NM\_033118) is another VGAM1793 host target gene. MYLK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYLK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYLK2 BINDING SITE, designated SEQ ID:26966, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59833] Another function of VGAM1793 is therefore inhibition of Myosin Light Chain Kinase 2, Skeletal Muscle (MYLK2, Ac-



cession NM\_033118). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYLK2. Myogenin (myogenic factor 4) (MYOG, Accession XM\_001688) is another VGAM1793 host target gene. MYOG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYOG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYOG BINDING SITE, designated SEQ ID:29848, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59834] Another function of VGAM1793 is therefore inhibition of Myogenin (myogenic factor 4) (MYOG, Accession XM\_001688), a gene which can induce myogenesis in a variety of cell types. Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYOG. The function of MYOG has been established by previous studies. Studies of the cloned MYF4 indicate limited sequence homology to MYOD1 and MYF5. Hybridization to DNA from a panel of somatic cell hybrids indicated that the MYF4 gene

is located on human chromosome 1 (Braun et al., 1989). By in situ hybridization to human metaphase chromosomes and by segregation analysis in interspecific somatic cell hybrid panels, Olson et al. (1990) assigned the MYOG gene to 1q31–q41 and showed that the corresponding genes in the mouse (Myog) and Chinese hamster (MYOG) mapped to regions of syntenic homology on mouse chromosome 1 and Chinese hamster chromosome 5. Nonlinkage to MYOD1, MYF5, and MYF6 (OMIM Ref. No. 159991) was demonstrated. Animal model experiments lend further support to the function of MYOG. Myogenin is a muscle-specific transcription factor that can induce myogenesis in a variety of cell types in tissue culture. It is a member of the basic helix–loop–helix (bHLH) gene family. To test its role in vivo, Hasty et al. (1993) generated mice homozygous for a targeted mutation in the myogenin gene. These mice survived fetal development but died immediately after birth and showed a severe reduction of all skeletal muscle. Thus, myogenin–mutant mice differed from mice carrying mutations in genes for the related MYF5 (OMIM Ref. No. 159990) and MYF3 (MYOD1; 159970), which have no muscle defects. From these observations, Hasty et al. (1993) concluded that myogenin is

essential for the development of functional skeletal muscle. Nabeshima et al. (1993) independently found similar results and arrived at similar conclusions from 'knockout' experiments in mice.

[59835] It is appreciated that the abovementioned animal model for MYOG is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[59836] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59837] Hasty, P.; Bradley, A.; Morris, J. H.; Edmondson, D. G.; Venuti, J. M.; Olson, E. N.; Klein, W. H. : Muscle deficiency and neonatal death in mice with a targeted mutation in the myogenin gene. Nature 364: 501–506, 1993. ; and

[59838] Braun, T.; Grzeschik, K.–H.; Bober, E.; Arnold, H.–H. : The MYF genes, a group of human muscle determining factors, are localized on different human chromosomes. (Abstract) Cytogenet.

[59839] Further studies establishing the function and utilities of MYOG are found in John Hopkins OMIM database record ID 159980, and in cited publications numbered 168 and 11143–1688 listed in the bibliography section hereinbe–

low, which are also hereby incorporated by reference. Neuregulin 1 (NRG1, Accession NM\_004495) is another VGAM1793 host target gene. NRG1 BINDING SITE1 through NRG1 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NRG1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRG1 BINDING SITE1 through NRG1 BINDING SITE4, designated SEQ ID:10834, SEQ ID:15137, SEQ ID:15138 and SEQ ID:15141 respectively, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59840] Another function of VGAM1793 is therefore inhibition of Neuregulin 1 (NRG1, Accession NM\_004495), a gene which is essential for neuronal development. Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRG1. The function of NRG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1259. Olfactomedin 1 (OLFM1, Accession NM\_006334) is another VGAM1793 host target gene.

OLFM1 BINDING SITE1 through OLFM1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OLFM1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OLFM1 BINDING SITE1 through OLFM1 BINDING SITE3, designated SEQ ID:13034, SEQ ID:27761 and SEQ ID:7497 respectively, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59841] Another function of VGAM1793 is therefore inhibition of Olfactomedin 1 (OLFM1, Accession NM\_006334). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OLFM1. SNL (Accession NM\_003088) is another VGAM1793 host target gene. SNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNL BINDING SITE, designated SEQ ID:9060, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4504.

[59842] Another function of VGAM1793 is therefore inhibition of SNL (Accession NM\_003088), a gene which organizes filamentous actin into bundles with a minimum of 4.1:1 actin/fascin ratio. Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNL. The function of SNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675. APEG1 (Accession XM\_050966) is another VGAM1793 host target gene. APEG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APEG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APEG1 BINDING SITE, designated SEQ ID:35693, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59843] Another function of VGAM1793 is therefore inhibition of APEG1 (Accession XM\_050966). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with APEG1. Cat Eye Syndrome Chromosome Region, Candidate 7 (CECR7, Accession XM\_086803) is another VGAM1793 host target gene. CECR7 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CECR7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CECR7 BINDING SITE, designated SEQ ID:38879, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59844] Another function of VGAM1793 is therefore inhibition of Cat Eye Syndrome Chromosome Region, Candidate 7 (CECR7, Accession XM\_086803). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR7. Complexin 1 (CPLX1, Accession NM\_006651) is another VGAM1793 host target gene. CPLX1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CPLX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of CPLX1 BINDING SITE, designated SEQ ID:13449, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59845] Another function of VGAM1793 is therefore inhibition of Complexin 1 (CPLX1, Accession NM\_006651). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPLX1. DKFZP434B205 (Accession XM\_059966) is another VGAM1793 host target gene. DKFZP434B205 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434B205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434B205 BINDING SITE, designated SEQ ID:37125, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59846] Another function of VGAM1793 is therefore inhibition of DKFZP434B205 (Accession XM\_059966). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated



with DKFZP434B205. DKFZP586J1624 (Accession NM\_015537) is another VGAM1793 host target gene. DKFZP586J1624 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586J1624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586J1624 BINDING SITE, designated SEQ ID:17799, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59847] Another function of VGAM1793 is therefore inhibition of DKFZP586J1624 (Accession NM\_015537). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586J1624. FLJ10342 (Accession NM\_018064) is another VGAM1793 host target gene. FLJ10342 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10342 BINDING SITE, designated SEQ ID:19835, to the

nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59848] Another function of VGAM1793 is therefore inhibition of FLJ10342 (Accession NM\_018064). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10342. FLJ10759 (Accession NM\_018207) is another VGAM1793 host target gene. FLJ10759 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10759 BINDING SITE, designated SEQ ID:20101, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59849] Another function of VGAM1793 is therefore inhibition of FLJ10759 (Accession NM\_018207). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10759. FLJ13052 (Accession NM\_023018) is another VGAM1793 host target gene. FLJ13052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ13052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13052 BINDING SITE, designated SEQ ID:23283, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59850] Another function of VGAM1793 is therefore inhibition of FLJ13052 (Accession NM\_023018). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13052. FLJ23511 (Accession NM\_032239) is another VGAM1793 host target gene. FLJ23511 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23511 BINDING SITE, designated SEQ ID:25967, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59851] Another function of VGAM1793 is therefore inhibition of FLJ23511 (Accession NM\_032239). Accordingly, utilities of

VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23511. HSPC154 (Accession NM\_014177) is another VGAM1793 host target gene. HSPC154 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HSPC154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC154 BINDING SITE, designated SEQ ID:15463, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59852] Another function of VGAM1793 is therefore inhibition of HSPC154 (Accession NM\_014177). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC154. HSU79274 (Accession NM\_013300) is another VGAM1793 host target gene. HSU79274 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HSU79274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

HSU79274 BINDING SITE, designated SEQ ID:14959, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59853] Another function of VGAM1793 is therefore inhibition of HSU79274 (Accession NM\_013300). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSU79274. KIAA0217 (Accession XM\_040265) is another VGAM1793 host target gene. KIAA0217 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0217, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0217 BINDING SITE, designated SEQ ID:33280, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59854] Another function of VGAM1793 is therefore inhibition of KIAA0217 (Accession XM\_040265). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0217. KIAA0848 (Accession NM\_014926) is another VGAM1793 host target gene. KIAA0848 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0848 BINDING SITE, designated SEQ ID:17214, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59855] Another function of VGAM1793 is therefore inhibition of KIAA0848 (Accession NM\_014926). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0848. KIAA1467 (Accession XM\_049605) is another VGAM1793 host target gene. KIAA1467 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1467, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1467 BINDING SITE, designated SEQ ID:35457, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59856] Another function of VGAM1793 is therefore inhibition of

KIAA1467 (Accession XM\_049605). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1467. KIAA1582 (Accession XM\_037262) is another VGAM1793 host target gene. KIAA1582 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1582, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1582 BINDING SITE, designated SEQ ID:32587, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59857] Another function of VGAM1793 is therefore inhibition of KIAA1582 (Accession XM\_037262). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1582. KIAA1784 (Accession XM\_036660) is another VGAM1793 host target gene. KIAA1784 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1784, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1784 BINDING SITE, designated SEQ ID:32484, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59858] Another function of VGAM1793 is therefore inhibition of KIAA1784 (Accession XM\_036660). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1784. KIAA1908 (Accession XM\_055834) is another VGAM1793 host target gene. KIAA1908 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1908 BINDING SITE, designated SEQ ID:36333, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59859] Another function of VGAM1793 is therefore inhibition of KIAA1908 (Accession XM\_055834). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1908. KLK15 (Accession NM\_138563) is another



VGAM1793 host target gene. KLK15 BINDING SITE1 and KLK15 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KLK15, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLK15 BINDING SITE1 and KLK15 BINDING SITE2, designated SEQ ID:28863 and SEQ ID:23265 respectively, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59860] Another function of VGAM1793 is therefore inhibition of KLK15 (Accession NM\_138563). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLK15. MIG (Accession NM\_002416) is another VGAM1793 host target gene. MIG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIG BINDING SITE, designated SEQ ID:8248, to the nucleotide sequence of VGAM1793 RNA, herein

designated VGAM RNA, also designated SEQ ID:4504.

[59861] Another function of VGAM1793 is therefore inhibition of MIG (Accession NM\_002416). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIG. NEU4 (Accession NM\_080741) is another VGAM1793 host target gene. NEU4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NEU4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEU4 BINDING SITE, designated SEQ ID:28027, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59862] Another function of VGAM1793 is therefore inhibition of NEU4 (Accession NM\_080741). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEU4. Prostate Cancer Associated Protein 7 (PCANAP7, Accession XM\_167803) is another VGAM1793 host target gene. PCANAP7 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by

PCANAP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCANAP7 BINDING SITE, designated SEQ ID:44837, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59863] Another function of VGAM1793 is therefore inhibition of Prostate Cancer Associated Protein 7 (PCANAP7, Accession XM\_167803). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCANAP7. SAST (Accession XM\_032034) is another VGAM1793 host target gene. SAST BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SAST, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SAST BINDING SITE, designated SEQ ID:31543, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59864] Another function of VGAM1793 is therefore inhibition of SAST (Accession XM\_032034). Accordingly, utilities of

VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAST. Solute Carrier Family 26, Member 9 (SLC26A9, Accession NM\_134325) is another VGAM1793 host target gene. SLC26A9 BINDING SITE1 and SLC26A9 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC26A9, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A9 BINDING SITE1 and SLC26A9 BINDING SITE2, designated SEQ ID:28631 and SEQ ID:27493 respectively, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59865] Another function of VGAM1793 is therefore inhibition of Solute Carrier Family 26, Member 9 (SLC26A9, Accession NM\_134325). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A9. LOC118611 (Accession XM\_061055) is another VGAM1793 host target gene. LOC118611 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC118611, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118611 BINDING SITE, designated SEQ ID:37187, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59866] Another function of VGAM1793 is therefore inhibition of LOC118611 (Accession XM\_061055). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118611. LOC145989 (Accession XM\_004815) is another VGAM1793 host target gene. LOC145989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145989 BINDING SITE, designated SEQ ID:29950, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59867] Another function of VGAM1793 is therefore inhibition of LOC145989 (Accession XM\_004815). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC145989. LOC148014 (Accession XM\_085999) is another VGAM1793 host target gene. LOC148014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148014 BINDING SITE, designated SEQ ID:38439, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59868] Another function of VGAM1793 is therefore inhibition of LOC148014 (Accession XM\_085999). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148014. LOC158435 (Accession NM\_138497) is another VGAM1793 host target gene. LOC158435 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158435 BINDING SITE, designated SEQ ID:28846, to

the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59869] Another function of VGAM1793 is therefore inhibition of LOC158435 (Accession NM\_138497). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158435. LOC158856 (Accession XM\_098998) is another VGAM1793 host target gene. LOC158856 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158856 BINDING SITE, designated SEQ ID:42035, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59870] Another function of VGAM1793 is therefore inhibition of LOC158856 (Accession XM\_098998). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158856. LOC163833 (Accession XM\_089174) is another VGAM1793 host target gene. LOC163833 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC163833, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163833 BINDING SITE, designated SEQ ID:39968, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59871] Another function of VGAM1793 is therefore inhibition of LOC163833 (Accession XM\_089174). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163833. LOC168667 (Accession XM\_166592) is another VGAM1793 host target gene. LOC168667 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC168667, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168667 BINDING SITE, designated SEQ ID:44569, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59872] Another function of VGAM1793 is therefore inhibition of LOC168667 (Accession XM\_166592). Accordingly, utilities



of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168667. LOC197319 (Accession XM\_113862) is another VGAM1793 host target gene. LOC197319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197319 BINDING SITE, designated SEQ ID:42477, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59873] Another function of VGAM1793 is therefore inhibition of LOC197319 (Accession XM\_113862). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197319. LOC202284 (Accession XM\_117372) is another VGAM1793 host target gene. LOC202284 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202284, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC202284 BINDING SITE, designated SEQ ID:43418, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59874] Another function of VGAM1793 is therefore inhibition of LOC202284 (Accession XM\_117372). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202284. LOC222183 (Accession XM\_168436) is another VGAM1793 host target gene. LOC222183 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222183 BINDING SITE, designated SEQ ID:45184, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59875] Another function of VGAM1793 is therefore inhibition of LOC222183 (Accession XM\_168436). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222183. LOC90120 (Accession XM\_029168) is another VGAM1793 host target gene. LOC90120 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90120 BINDING SITE, designated SEQ ID:30852, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59876] Another function of VGAM1793 is therefore inhibition of LOC90120 (Accession XM\_029168). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90120. LOC90499 (Accession XM\_032170) is another VGAM1793 host target gene. LOC90499 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90499 BINDING SITE, designated SEQ ID:31584, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59877] Another function of VGAM1793 is therefore inhibition of

LOC90499 (Accession XM\_032170). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90499. LOC96652 (Accession XM\_037474) is another VGAM1793 host target gene. LOC96652 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC96652, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC96652 BINDING SITE, designated SEQ ID:32627, to the nucleotide sequence of VGAM1793 RNA, herein designated VGAM RNA, also designated SEQ ID:4504.

[59878] Another function of VGAM1793 is therefore inhibition of LOC96652 (Accession XM\_037474). Accordingly, utilities of VGAM1793 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC96652. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1794 (VGAM1794) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[59879] VGAM1794 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1794 was detected is described hereinabove with reference to Figs. 1–8.

[59880] VGAM1794 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1794 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59881] VGAM1794 gene encodes a VGAM1794 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1794 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1794 precursor RNA is designated SEQ ID:1780, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1780 is located at position 84588 relative to the genome of Rana Tigrina Ranavirus.

[59882] VGAM1794 precursor RNA folds onto itself, forming VGAM1794 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59883] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1794 folded precursor RNA into VGAM1794 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1794 RNA is designated SEQ ID:4505, and is provided hereinbelow with reference to the sequence listing part.

[59884] VGAM1794 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1794 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1794 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[59885] VGAM1794 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1794 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1794 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1794 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1794 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[59886] The complementary binding of VGAM1794 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1794 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1794 host target RNA into VGAM1794 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59887] It is appreciated that VGAM1794 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1794 host target genes. The mRNA of each one of this plurality of VGAM1794 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1794 RNA, herein designated VGAM RNA, and which when bound by VGAM1794 RNA causes inhibition of translation of respective one or more VGAM1794 host target proteins.

[59888] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1794 gene, herein designated VGAM GENE, on one



or more VGAM1794 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59889] It is yet further appreciated that a function of VGAM1794 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1794 correlate with, and may be deduced from, the identity of the host target genes which VGAM1794 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59890] Nucleotide sequences of the VGAM1794 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1794 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1794 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1794 are further described hereinbelow with reference to Table 1.

[59891] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1794 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1794 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59892] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1794 gene, herein designated VGAM is inhibition of expression of VGAM1794 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1794 correlate with, and may be deduced from, the identity of the target genes which VGAM1794 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59893] Alkaline Phosphatase, Intestinal (ALPI, Accession

NM\_001631) is a VGAM1794 host target gene. ALPI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALPI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALPI BINDING SITE, designated SEQ ID:7343, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59894] A function of VGAM1794 is therefore inhibition of Alkaline Phosphatase, Intestinal (ALPI, Accession NM\_001631), a gene which is a glycoprotein phosphatase. Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALPI. The function of ALPI and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM885. Alkaline Phosphatase, Placental (Regan isozyme) (ALPP, Accession XM\_044131) is another VGAM1794 host target gene. ALPP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALPP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALPP BINDING SITE, designated SEQ ID:34138, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59895] Another function of VGAM1794 is therefore inhibition of Alkaline Phosphatase, Placental (Regan isozyme) (ALPP, Accession XM\_044131), a gene which is a placental alkaline phosphatase. Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALPP. The function of ALPP has been established by previous studies. Boyer (1961, 1963) described an electrophoretic variant of alkaline phosphatase (orthophosphoric monoester phosphohydrolase, alkaline optimum; EC 3.1.3.1), which appears in the serum during pregnancy in some women, and demonstrated its origin in the placenta. Since the human placenta is largely fetal in origin, the polymorphism may be a characteristic determined by the fetal genotype. Historically, this was the first described example of a polymorphic placental protein. Robson and Harris (1965) studied the genetics. Beckman et al. (1967) found a rare phenotype, absence of placental alkaline phosphatase, in

twins and suggested that these twins might be homozygous for a 'silent allele' ('null allele'). The twins were also concordant for Crouzon craniofacial dysostosis (OMIM Ref. No. 123500), raising the question of a causal relationship. Palmarino et al. (1979) found evidence for at least 11 different mutant alleles at the placental alkaline phosphatase locus. Garattini et al. (1985) demonstrated 'appreciable amounts' of placental alkaline phosphatase in extracts of liver and intestine. Kam et al. (1985) cloned placental alkaline phosphatase cDNA, sequenced it, and mapped the gene by direct spot-blot hybridization to the DNA of chromosomes resolved by dual laser chromosome sorting. A strong signal was obtained with chromosome 2. With longer exposure, a weaker signal appeared also on chromosome 17. They speculated that PLAP-related gene(s) may be located there. Human testis and thymus contain small amounts of an ALP closely resembling, but not identical to, placental ALP. This ALP has been referred to as placental-like ALP or the Nagao isoenzyme (Henthorn et al., 1987); see 171810. Millan and Stigbrand (1983) maintained that placental-like ALP was probably the product of a separate locus. Martin et al. (1987) used a cDNA probe in Southern blot analysis of somatic cell hybrid DNA and

in situ hybridization to locate PLAP to 2q37. Martin et al. (1987) described a RFLP of the PLAP gene. Griffin et al. (1987) mapped both the placental and the intestinal alkaline phosphatase genes to 2q34–q37 by chromosomal in situ hybridization and hybridization to the DNA of somatic cell hybrids. By in situ hybridization, Raimondi et al. (1988) assigned the ALPP gene to 2q37. Knoll et al. (1988) concluded that 3 closely related alkaline phosphatase genes reside on the long arm of chromosome 2 in man. One of these genes (PLAP; the placental ALP–1, in their symbology) encodes the classic heat-stabile placental alkaline phosphatase; a second (which they referred to as placental ALP–2) is closely related to the first, and may encode the so-called placental ALP-like enzyme of the testis and thymus; the third member of this gene family, the intestinal ALP gene, encodes intestinal alkaline phosphatase (OMIM Ref. No. 171740). The expression of the intestinal and placental genes is highly tissue-specific in spite of nearly 90% sequence similarity within their exons. Knoll et al. (1988) compared the placental alkaline phosphatase gene with the placental-like gene.

[59896] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

[59897] Beckman, L.; Beckman, G.; Christodoulou, C.; Ifekwu-nigwe, A. : Variations in human placental alkaline phosphatase. *Acta Genet. Statist. Med.* 17: 406–412, 1967. ; and

[59898] Knoll, B. J.; Rothblum, K. N.; Longley, M. : Nucleotide sequence of the human placental alkaline phosphatase gene: evolution of the 5-prime flanking region by deletion/substitution. *J.*

[59899] Further studies establishing the function and utilities of ALPP are found in John Hopkins OMIM database record ID 171800, and in cited publications numbered 3253–3256, 3499, 3503–3507, 2498, 3508, 3509–351 and 3780 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mannosidase, Alpha, Class 2A, Member 2 (MAN2A2, Accession NM\_006122) is another VGAM1794 host target gene. MAN2A2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAN2A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN2A2 BINDING SITE, designated SEQ

ID:12765, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59900] Another function of VGAM1794 is therefore inhibition of Mannosidase, Alpha, Class 2A, Member 2 (MAN2A2, Accession NM\_006122), a gene which is an enzyme involved in the processing of N-linked glycans. Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN2A2. The function of MAN2A2 has been established by previous studies. Golgi alpha-mannosidase II (OMIM Ref. No. 154582) is an enzyme involved in the processing of N-linked glycans. Using a previously isolated murine cDNA clone as a probe, Misago et al. (1995) isolated cDNA clones encompassing the human MANA2 cDNA open reading frame. During the isolation of genomic clones, genes related to that encoding alpha-mannosidase II were isolated. One such gene was found to encode an isozyme, which they designated alpha-mannosidase II(x). A 5-kb cDNA clone of the MANA2X gene was then isolated from a human melanoma cDNA library. Comparison between the MANA2X and MANA2 cDNAs suggested that the cloned cDNA encodes a truncated



polypeptide with 796 amino acid residues, while the product of the MANA2 gene consists of 1144 amino acid residues. However, further studies indicated that alternative splicing of the MANA2X transcript can result in an additional transcript encoding an 1139-amino acid polypeptide. Northern analysis showed transcription of MANA2X in various tissues, suggesting that it is a housekeeping gene. COS cells transfected with MANA2X cDNA containing the full-length open reading frame showed an increase in alpha-mannosidase activity. Animal model experiments lend further support to the function of MAN2A2. Akama et al. (2002) generated mice deficient for the Man2a2 gene, which encodes alpha-mannosidase-IIx, an enzyme that forms intermediate asparagine-linked carbohydrates (N-glycans). Male mice lacking Man2a2 are largely infertile. The Man2a2-null spermatogenic cells fail to adhere to Sertoli cells and are prematurely released from the testis to the epididymis. Akama et al. (2002) identified an N-glycan structure that plays a key role in germ cell-Sertoli cell adhesion and identified a specific carbohydrate that is required for spermatogenesis. This carbohydrate is designated 310.11 and is an N-acetylglucosamine-terminated tri-antennary and fucosy-

lated N-glycan structure.

[59901] It is appreciated that the abovementioned animal model for MAN2A2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[59902] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[59903] Misago, M.; Liao, Y.-F.; Kudo, S.; Eto, S.; Mattei, M.-G.; Moremen, K. W.; Fukuda, M. N. : Molecular cloning and expression of cDNAs encoding human alpha-mannosidase II and a previously unrecognized alpha-mannosidase II(X) isozyme. Proc. Nat. Acad. Sci. 92: 11766-11770, 1995. ; and

[59904] Akama, T. O.; Nakagawa, H.; Sugihara, K.; Narisawa, S.; Ohyama, C.; Nishimura, S.-I.; O'Brien, D. A.; Moremen, K. W.; Millan, J. L.; Fukuda, M. N. : Germ cell survival through carbohydra.

[59905] Further studies establishing the function and utilities of MAN2A2 are found in John Hopkins OMIM database record ID 600988, and in cited publications numbered 716 and 11529 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Parkinson

Disease (autosomal recessive, juvenile) 2, Parkin (PARK2, Accession NM\_013987) is another VGAM1794 host target gene. PARK2 BINDING SITE1 through PARK2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PARK2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PARK2 BINDING SITE1 through PARK2 BINDING SITE3, designated SEQ ID:15151, SEQ ID:15158 and SEQ ID:10904 respectively, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59906] Another function of VGAM1794 is therefore inhibition of Parkinson Disease (autosomal recessive, juvenile) 2, Parkin (PARK2, Accession NM\_013987). Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PARK2. FLJ10352 (Accession NM\_032142) is another VGAM1794 host target gene. FLJ10352 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10352 BINDING SITE, designated SEQ ID:25824, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59907] Another function of VGAM1794 is therefore inhibition of FLJ10352 (Accession NM\_032142). Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10352. KIAA0935 (Accession XM\_052620) is another VGAM1794 host target gene. KIAA0935 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0935 BINDING SITE, designated SEQ ID:36010, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59908] Another function of VGAM1794 is therefore inhibition of KIAA0935 (Accession XM\_052620). Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0935. KIAA1061 (Accession XM\_048786) is another VGAM1794 host target gene. KIAA1061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1061 BINDING SITE, designated SEQ ID:35265, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59909] Another function of VGAM1794 is therefore inhibition of KIAA1061 (Accession XM\_048786). Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1061. KIAA1750 (Accession XM\_043067) is another VGAM1794 host target gene. KIAA1750 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1750 BINDING SITE, designated SEQ ID:33873, to the nucleotide sequence of VGAM1794 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4505.

[59910] Another function of VGAM1794 is therefore inhibition of KIAA1750 (Accession XM\_043067). Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1750. KIAA1881 (Accession XM\_170901) is another VGAM1794 host target gene. KIAA1881 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1881 BINDING SITE, designated SEQ ID:45654, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59911] Another function of VGAM1794 is therefore inhibition of KIAA1881 (Accession XM\_170901). Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1881. Mitogen-activated Protein Kinase-activated Protein Kinase 2 (MAPKAPK2, Accession NM\_004759) is another VGAM1794 host target gene. MAPKAPK2 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by MAPKAPK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPKAPK2 BINDING SITE, designated SEQ ID:11148, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59912] Another function of VGAM1794 is therefore inhibition of Mitogen-activated Protein Kinase-activated Protein Kinase 2 (MAPKAPK2, Accession NM\_004759). Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPKAPK2. Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM\_144564) is another VGAM1794 host target gene. SLC39A3 BINDING SITE1 and SLC39A3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC39A3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC39A3 BINDING SITE1 and SLC39A3 BINDING SITE2, designated SEQ ID:29354 and SEQ ID:29355 respectively, to the nucleotide sequence of

VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59913] Another function of VGAM1794 is therefore inhibition of Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM\_144564). Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC39A3. LOC51134 (Accession NM\_016122) is another VGAM1794 host target gene. LOC51134 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51134 BINDING SITE, designated SEQ ID:18209, to the nucleotide sequence of VGAM1794 RNA, herein designated VGAM RNA, also designated SEQ ID:4505.

[59914] Another function of VGAM1794 is therefore inhibition of LOC51134 (Accession NM\_016122). Accordingly, utilities of VGAM1794 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51134. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the



present invention, referred to here as Viral Genomic Address Messenger 1795 (VGAM1795) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59915] VGAM1795 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1795 was detected is described hereinabove with reference to Figs. 1–8.

[59916] VGAM1795 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1795 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59917] VGAM1795 gene encodes a VGAM1795 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1795 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1795 precursor RNA is designated SEQ ID:1781, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1781 is located at position 85710 relative to the

genome of Rana Tigrina Ranavirus.

[59918] VGAM1795 precursor RNA folds onto itself, forming VGAM1795 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59919] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1795 folded precursor RNA into VGAM1795 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1795 RNA is designated SEQ ID:4506, and is provided hereinbelow with reference to the sequence listing part.

[59920] VGAM1795 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1795 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1795 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59921] VGAM1795 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1795 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1795 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1795 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1795 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59922] The complementary binding of VGAM1795 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1795 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1795 host target RNA into VGAM1795 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59923] It is appreciated that VGAM1795 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1795 host target genes. The mRNA of each one of this plurality of VGAM1795 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1795 RNA, herein designated VGAM RNA, and which when bound by VGAM1795 RNA causes inhibition of translation of respective one or more VGAM1795 host target proteins.

[59924] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1795 gene, herein designated VGAM GENE, on one or more VGAM1795 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59925] It is yet further appreciated that a function of VGAM1795 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1795 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1795

correlate with, and may be deduced from, the identity of the host target genes which VGAM1795 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59926] Nucleotide sequences of the VGAM1795 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1795 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1795 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1795 are further described hereinbelow with reference to Table 1.

[59927] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1795 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1795 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59928] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1795 gene, herein designated VGAM is inhibition of expression of VGAM1795 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1795 correlate with, and may be deduced

from, the identity of the target genes which VGAM1795 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59929] LOC157663 (Accession XM\_088354) is a VGAM1795 host target gene. LOC157663 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157663 BINDING SITE, designated SEQ ID:39638, to the nucleotide sequence of VGAM1795 RNA, herein designated VGAM RNA, also designated SEQ ID:4506.

[59930] A function of VGAM1795 is therefore inhibition of LOC157663 (Accession XM\_088354). Accordingly, utilities of VGAM1795 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157663. LOC254228 (Accession XM\_171123) is another VGAM1795 host target gene. LOC254228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC254228 BINDING SITE, designated SEQ ID:45919, to the nucleotide sequence of VGAM1795 RNA, herein designated VGAM RNA, also designated SEQ ID:4506.

[59931] Another function of VGAM1795 is therefore inhibition of LOC254228 (Accession XM\_171123). Accordingly, utilities of VGAM1795 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254228. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1796 (VGAM1796) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59932] VGAM1796 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1796 was detected is described hereinabove with reference to Figs. 1–8.

[59933] VGAM1796 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1796 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[59934] VGAM1796 gene encodes a VGAM1796 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1796 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1796 precursor RNA is designated SEQ ID:1782, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1782 is located at position 79650 relative to the genome of Rana Tigrina Ranavirus.

[59935] VGAM1796 precursor RNA folds onto itself, forming VGAM1796 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59936] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1796 folded precursor RNA into VGAM1796 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1796 RNA is designated SEQ ID:4507, and is provided hereinbelow with reference to the sequence listing part.

[59937] VGAM1796 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1796 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1796 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59938] VGAM1796 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1796 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1796 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1796 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1796 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59939] The complementary binding of VGAM1796 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1796 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1796 host target RNA into VGAM1796 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59940] It is appreciated that VGAM1796 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1796 host target genes. The mRNA of each one of this plurality of VGAM1796 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1796 RNA, herein designated VGAM RNA, and which when bound by VGAM1796 RNA causes inhibition of translation of respective one or more VGAM1796 host target proteins.

[59941] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1796 gene, herein designated VGAM GENE, on one or more VGAM1796 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59942] It is yet further appreciated that a function of VGAM1796 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1796 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1796 correlate with, and may be deduced from, the identity of the host target genes which VGAM1796 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59943] Nucleotide sequences of the VGAM1796 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1796 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1796 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1796 are further described hereinbelow with reference to Table 1.

[59944] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1796 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1796 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59945] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1796 gene, herein designated VGAM is inhibition of expression of VGAM1796 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1796 correlate with, and may be deduced from, the identity of the target genes which VGAM1796 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59946] Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM\_018956) is a VGAM1796 host target gene. C9orf9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C9orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf9 BINDING SITE, designated SEQ ID:21027, to the nucleotide sequence of VGAM1796 RNA, herein designated VGAM RNA, also designated SEQ ID:4507.

[59947] A function of VGAM1796 is therefore inhibition of Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM\_018956). Accordingly, utilities of VGAM1796 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf9. KIAA0472 (Accession XM\_050147) is another VGAM1796 host target gene. KIAA0472 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0472, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0472 BINDING SITE, designated SEQ ID:35577, to the nucleotide sequence of VGAM1796 RNA, herein designated VGAM RNA, also designated SEQ ID:4507.

[59948] Another function of VGAM1796 is therefore inhibition of KIAA0472 (Accession XM\_050147). Accordingly, utilities of VGAM1796 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0472. LOC158402 (Accession XM\_098936) is another VGAM1796 host target gene. LOC158402 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158402, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158402 BINDING SITE, designated SEQ ID:41975, to the nucleotide sequence of VGAM1796 RNA, herein designated VGAM RNA, also designated SEQ ID:4507.

[59949] Another function of VGAM1796 is therefore inhibition of LOC158402 (Accession XM\_098936). Accordingly, utilities of VGAM1796 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158402. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1797 (VGAM1797) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[59950] VGAM1797 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1797 was detected is described hereinabove with reference to Figs. 1-8.

[59951] VGAM1797 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus.



VGAM1797 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[59952] VGAM1797 gene encodes a VGAM1797 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1797 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1797 precursor RNA is designated SEQ ID:1783, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1783 is located at position 82741 relative to the genome of Rana Tigrina Ranavirus.

[59953] VGAM1797 precursor RNA folds onto itself, forming VGAM1797 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[59954] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1797 folded precursor RNA into VGAM1797 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM1797 RNA is designated SEQ ID:4508, and is provided hereinbelow with reference to the sequence listing part.

[59955] VGAM1797 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1797 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1797 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[59956] VGAM1797 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1797 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1797 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1797 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1797 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[59957] The complementary binding of VGAM1797 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1797 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1797 host target RNA into VGAM1797 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[59958] It is appreciated that VGAM1797 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1797 host target genes. The mRNA of each one of this plurality of VGAM1797 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1797 RNA, herein designated VGAM RNA, and which when bound by VGAM1797 RNA causes inhibition of translation of respective one or more VGAM1797 host target proteins.

[59959] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1797 gene, herein designated VGAM GENE, on one or more VGAM1797 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[59960] It is yet further appreciated that a function of VGAM1797 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1797 correlate with, and may be deduced from, the identity of the host target genes which VGAM1797 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[59961] Nucleotide sequences of the VGAM1797 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1797 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1797 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1797 are further described hereinbelow with reference to Table 1.

[59962] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1797 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1797 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[59963] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1797 gene, herein designated VGAM is inhibition of expression of VGAM1797 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1797 correlate with, and may be deduced from, the identity of the target genes which VGAM1797 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[59964] Ankyrin-like with Transmembrane Domains 1 (ANKTM1, Accession NM\_007332) is a VGAM1797 host target gene. ANKTM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKTM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKTM1 BINDING SITE, designated SEQ

ID:14258, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59965] A function of VGAM1797 is therefore inhibition of Ankyrin-like with Transmembrane Domains 1 (ANKTM1, Accession NM\_007332), a gene which attaches integral membrane proteins to cytoskeletal elements. Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKTM1. The function of ANKTM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM644. Copine III (CPNE3, Accession NM\_003909) is another VGAM1797 host target gene. CPNE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPNE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPNE3 BINDING SITE, designated SEQ ID:9996, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59966] Another function of VGAM1797 is therefore inhibition of

Copine III (CPNE3, Accession NM\_003909), a gene which may function in membrane trafficking. Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPNE3. The function of CPNE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. Dual Specificity Phosphatase 5 (DUSP5, Accession NM\_004419) is another VGAM1797 host target gene. DUSP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DUSP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP5 BINDING SITE, designated SEQ ID:10684, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59967] Another function of VGAM1797 is therefore inhibition of Dual Specificity Phosphatase 5 (DUSP5, Accession NM\_004419), a gene which displays phosphatase activity toward several substrates. Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment



of diseases and clinical conditions associated with DUSP5. The function of DUSP5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM538. Guanylate Cyclase 1, Soluble, Beta 2 (GUCY1B2, Accession NM\_004129) is another VGAM1797 host target gene. GUCY1B2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GUCY1B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GUCY1B2 BINDING SITE, designated SEQ ID:10336, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59968] Another function of VGAM1797 is therefore inhibition of Guanylate Cyclase 1, Soluble, Beta 2 (GUCY1B2, Accession NM\_004129), a gene which is beta 2 subunit of soluble guanylate cyclase which converts GTP into the second messenger cGMP and plays a major role in the cardiovascular system as a receptor for nitric oxide. Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with GUCY1B2. The function of GUCY1B2 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM379. Neuralized-like (Drosophila) (NEURL, Accession NM\_004210) is another VGAM1797 host target gene. NEURL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEURL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEURL BINDING SITE, designated SEQ ID:10414, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59969] Another function of VGAM1797 is therefore inhibition of Neuralized-like (Drosophila) (NEURL, Accession NM\_004210). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEURL. RAB6A, Member RAS Oncogene Family (RAB6A, Accession NM\_002869) is another VGAM1797 host target gene. RAB6A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB6A, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB6A BINDING SITE, designated SEQ ID:8778, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59970] Another function of VGAM1797 is therefore inhibition of RAB6A, Member RAS Oncogene Family (RAB6A, Accession NM\_002869), a gene which is involved in protein trafficking. Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB6A. The function of RAB6A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. Regulator of G-protein Signalling 5 (RGS5, Accession NM\_003617) is another VGAM1797 host target gene. RGS5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS5 BINDING SITE, designated SEQ ID:9679, to the nucleotide se-

quence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59971] Another function of VGAM1797 is therefore inhibition of Regulator of G-protein Signalling 5 (RGS5, Accession NM\_003617). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS5. Synaptosomal-associated Protein, 23kDa (SNAP23, Accession NM\_003825) is another VGAM1797 host target gene. SNAP23 BINDING SITE1 and SNAP23 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SNAP23, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAP23 BINDING SITE1 and SNAP23 BINDING SITE2, designated SEQ ID:9921 and SEQ ID:28286 respectively, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59972] Another function of VGAM1797 is therefore inhibition of Synaptosomal-associated Protein, 23kDa (SNAP23, Accession NM\_003825), a gene which is essential component of the high affinity receptor for the general membrane fusion

machinery. Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAP23. The function of SNAP23 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1533. Zinc Finger Protein 264 (ZNF264, Accession NM\_003417) is another VGAM1797 host target gene. ZNF264 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF264, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF264 BINDING SITE, designated SEQ ID:9457, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59973] Another function of VGAM1797 is therefore inhibition of Zinc Finger Protein 264 (ZNF264, Accession NM\_003417). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF264. ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Acces-

sion XM\_031949) is another VGAM1797 host target gene. ACTR1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ACTR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACTR1A BINDING SITE, designated SEQ ID:31531, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59974] Another function of VGAM1797 is therefore inhibition of ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Accession XM\_031949). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACTR1A. Activating Transcription Factor 3 (ATF3, Accession NM\_004024) is another VGAM1797 host target gene. ATF3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATF3 BINDING SITE, designated SEQ ID:10243,

to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59975] Another function of VGAM1797 is therefore inhibition of Activating Transcription Factor 3 (ATF3, Accession NM\_004024). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATF3. BANK (Accession NM\_017935) is another VGAM1797 host target gene. BANK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BANK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BANK BINDING SITE, designated SEQ ID:19626, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59976] Another function of VGAM1797 is therefore inhibition of BANK (Accession NM\_017935). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BANK. Chromosome 8 Open Reading Frame 2 (C8orf2, Accession NM\_007175) is another VGAM1797 host target gene. C8orf2 BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by C8orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf2 BINDING SITE, designated SEQ ID:14023, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59977] Another function of VGAM1797 is therefore inhibition of Chromosome 8 Open Reading Frame 2 (C8orf2, Accession NM\_007175). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf2. Cell Adhesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM\_006614) is another VGAM1797 host target gene. CHL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHL1 BINDING SITE, designated SEQ ID:13393, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ



ID:4508.

[59978] Another function of VGAM1797 is therefore inhibition of Cell Adhesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM\_006614). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHL1. COE2 (Accession XM\_034639) is another VGAM1797 host target gene. COE2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COE2 BINDING SITE, designated SEQ ID:32130, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59979] Another function of VGAM1797 is therefore inhibition of COE2 (Accession XM\_034639). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COE2. Death-associated Protein Kinase 2 (DA PK2, Accession NM\_014326) is another VGAM1797 host target gene. DAPK2 BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by DAPK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAPK2 BINDING SITE, designated SEQ ID:15636, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59980] Another function of VGAM1797 is therefore inhibition of Death-associated Protein Kinase 2 (DAPK2, Accession NM\_014326). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAPK2. ERAP140 (Accession XM\_059748) is another VGAM1797 host target gene. ERAP140 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ERAP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERAP140 BINDING SITE, designated SEQ ID:37087, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59981] Another function of VGAM1797 is therefore inhibition of ERAP140 (Accession XM\_059748). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERAP140. FLJ10201 (Accession NM\_018023) is another VGAM1797 host target gene. FLJ10201 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10201 BINDING SITE, designated SEQ ID:19764, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59982] Another function of VGAM1797 is therefore inhibition of FLJ10201 (Accession NM\_018023). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10201. FLJ30567 (Accession NM\_145022) is another VGAM1797 host target gene. FLJ30567 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ30567, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30567 BINDING SITE, designated SEQ ID:29633, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59983] Another function of VGAM1797 is therefore inhibition of FLJ30567 (Accession NM\_145022). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30567. Glutamic Pyruvate Transaminase (alanine aminotransferase) 2 (GPT2, Accession NM\_133443) is another VGAM1797 host target gene. GPT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPT2 BINDING SITE, designated SEQ ID:28526, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59984] Another function of VGAM1797 is therefore inhibition of Glutamic Pyruvate Transaminase (alanine aminotransferase) 2 (GPT2, Accession NM\_133443). Accordingly, util-

ities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPT2. HIC (Accession XM\_041273) is another VGAM1797 host target gene. HIC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HIC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC BINDING SITE, designated SEQ ID:33495, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59985] Another function of VGAM1797 is therefore inhibition of HIC (Accession XM\_041273). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC. High Mobility Group Nucleosomal Binding Domain 4 (HMGN4, Accession NM\_006353) is another VGAM1797 host target gene. HMGN4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HMGN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of HMGN4 BINDING SITE, designated SEQ ID:13048, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59986] Another function of VGAM1797 is therefore inhibition of High Mobility Group Nucleosomal Binding Domain 4 (HMGN4, Accession NM\_006353). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGN4. HSPC039 (Accession NM\_016097) is another VGAM1797 host target gene. HSPC039 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC039, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC039 BINDING SITE, designated SEQ ID:18181, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59987] Another function of VGAM1797 is therefore inhibition of HSPC039 (Accession NM\_016097). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

HSPC039. KIAA0637 (Accession NM\_014838) is another VGAM1797 host target gene. KIAA0637 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0637, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0637 BINDING SITE, designated SEQ ID:16861, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59988] Another function of VGAM1797 is therefore inhibition of KIAA0637 (Accession NM\_014838). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0637. KIAA1136 (Accession XM\_166110) is another VGAM1797 host target gene. KIAA1136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1136 BINDING SITE, designated SEQ ID:43885, to the nucleotide sequence of VGAM1797 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4508.

[59989] Another function of VGAM1797 is therefore inhibition of KIAA1136 (Accession XM\_166110). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1136. KIAA1464 (Accession XM\_043069) is another VGAM1797 host target gene. KIAA1464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1464 BINDING SITE, designated SEQ ID:33885, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59990] Another function of VGAM1797 is therefore inhibition of KIAA1464 (Accession XM\_043069). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1464. KIAA1948 (Accession XM\_091984) is another VGAM1797 host target gene. KIAA1948 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1948, corresponding to



a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1948 BINDING SITE, designated SEQ ID:40082, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59991] Another function of VGAM1797 is therefore inhibition of KIAA1948 (Accession XM\_091984). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1948. LBP-9 (Accession NM\_014553) is another VGAM1797 host target gene. LBP-9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LBP-9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LBP-9 BINDING SITE, designated SEQ ID:15879, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59992] Another function of VGAM1797 is therefore inhibition of LBP-9 (Accession NM\_014553). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LBP-9. MacGAP (Accession NM\_033515) is another VGAM1797 host target gene. MacGAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MacGAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MacGAP BINDING SITE, designated SEQ ID:27288, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59993] Another function of VGAM1797 is therefore inhibition of MacGAP (Accession NM\_033515). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MacGAP. MGC5242 (Accession NM\_024033) is another VGAM1797 host target gene. MGC5242 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC5242, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5242 BINDING SITE, designated SEQ ID:23463, to the nucleotide

sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59994] Another function of VGAM1797 is therefore inhibition of MGC5242 (Accession NM\_024033). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5242. N4BP2 (Accession NM\_018177) is another VGAM1797 host target gene. N4BP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by N4BP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP2 BINDING SITE, designated SEQ ID:20004, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59995] Another function of VGAM1797 is therefore inhibition of N4BP2 (Accession NM\_018177). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP2. Olfactomedin 3 (OLFM3, Accession XM\_088951) is another VGAM1797 host target gene. OLFM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by OLFM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OLFM3 BINDING SITE, designated SEQ ID:39960, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59996] Another function of VGAM1797 is therefore inhibition of Olfactomedin 3 (OLFM3, Accession XM\_088951). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OLFM3. PRO2133 (Accession NM\_018619) is another VGAM1797 host target gene. PRO2133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2133 BINDING SITE, designated SEQ ID:20692, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59997] Another function of VGAM1797 is therefore inhibition of PRO2133 (Accession NM\_018619). Accordingly, utilities of

VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2133. RAB6C, Member RAS Oncogene Family (RAB6C, Accession NM\_032144) is another VGAM1797 host target gene. RAB6C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB6C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB6C BINDING SITE, designated SEQ ID:25835, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59998] Another function of VGAM1797 is therefore inhibition of RAB6C, Member RAS Oncogene Family (RAB6C, Accession NM\_032144). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB6C. Ribosomal Protein S6 Kinase, 52kDa, Polypeptide 1 (RPS6KC1, Accession NM\_012424) is another VGAM1797 host target gene. RPS6KC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPS6KC1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPS6KC1 BINDING SITE, designated SEQ ID:14801, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[59999] Another function of VGAM1797 is therefore inhibition of Ribosomal Protein S6 Kinase, 52kDa, Polypeptide 1 (RPS6KC1, Accession NM\_012424). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPS6KC1. SE57-1 (Accession NM\_025214) is another VGAM1797 host target gene. SE57-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SE57-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SE57-1 BINDING SITE, designated SEQ ID:24889, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60000] Another function of VGAM1797 is therefore inhibition of SE57-1 (Accession NM\_025214). Accordingly, utilities of

VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SE57-1. TED (Accession NM\_015686) is another VGAM1797 host target gene. TED BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TED, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TED BINDING SITE, designated SEQ ID:17921, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60001] Another function of VGAM1797 is therefore inhibition of TED (Accession NM\_015686). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TED. TTY7 (Accession NM\_031926) is another VGAM1797 host target gene. TTY7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TTY7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTY7 BINDING SITE, designated SEQ

ID:25673, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60002] Another function of VGAM1797 is therefore inhibition of TTY7 (Accession NM\_031926). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTY7. Wingless-type MMTV Integration Site Family, Member 16 (WNT16, Accession NM\_016087) is another VGAM1797 host target gene. WNT16 BINDING SITE1 and WNT16 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WNT16, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT16 BINDING SITE1 and WNT16 BINDING SITE2, designated SEQ ID:18172 and SEQ ID:27676 respectively, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60003] Another function of VGAM1797 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 16 (WNT16, Accession NM\_016087). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment



of diseases and clinical conditions associated with WNT16. Zinc Finger Protein 347 (ZNF347, Accession NM\_032584) is another VGAM1797 host target gene. ZNF347 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF347, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF347 BINDING SITE, designated SEQ ID:26319, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60004] Another function of VGAM1797 is therefore inhibition of Zinc Finger Protein 347 (ZNF347, Accession NM\_032584). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF347. LOC153516 (Accession NM\_138491) is another VGAM1797 host target gene. LOC153516 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153516, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153516 BINDING SITE, desig-

nated SEQ ID:28842, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60005] Another function of VGAM1797 is therefore inhibition of LOC153516 (Accession NM\_138491). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153516. LOC160646 (Accession XM\_090413) is another VGAM1797 host target gene. LOC160646 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC160646, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160646 BINDING SITE, designated SEQ ID:40001, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60006] Another function of VGAM1797 is therefore inhibition of LOC160646 (Accession XM\_090413). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160646. LOC200609 (Accession XM\_117256) is another VGAM1797 host target gene. LOC200609 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43334, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60007] Another function of VGAM1797 is therefore inhibition of LOC200609 (Accession XM\_117256). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. LOC221069 (Accession XM\_167676) is another VGAM1797 host target gene. LOC221069 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221069, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221069 BINDING SITE, designated SEQ ID:44768, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60008] Another function of VGAM1797 is therefore inhibition of

LOC221069 (Accession XM\_167676). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221069. LOC255461 (Accession XM\_173207) is another VGAM1797 host target gene. LOC255461 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255461 BINDING SITE, designated SEQ ID:46466, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60009] Another function of VGAM1797 is therefore inhibition of LOC255461 (Accession XM\_173207). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255461. LOC255516 (Accession XM\_173212) is another VGAM1797 host target gene. LOC255516 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255516, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC255516 BINDING SITE, designated SEQ ID:46472, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60010] Another function of VGAM1797 is therefore inhibition of LOC255516 (Accession XM\_173212). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255516. LOC51020 (Accession NM\_016063) is another VGAM1797 host target gene. LOC51020 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51020 BINDING SITE, designated SEQ ID:18138, to the nucleotide sequence of VGAM1797 RNA, herein designated VGAM RNA, also designated SEQ ID:4508.

[60011] Another function of VGAM1797 is therefore inhibition of LOC51020 (Accession NM\_016063). Accordingly, utilities of VGAM1797 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51020. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1798 (VGAM1798) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60012] VGAM1798 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1798 was detected is described hereinabove with reference to Figs. 1–8.

[60013] VGAM1798 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1798 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60014] VGAM1798 gene encodes a VGAM1798 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1798 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1798 precursor RNA is designated SEQ ID:1784, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1784 is located at position 85493 relative to the genome of Rana Tigrina Ranavirus.

[60015] VGAM1798 precursor RNA folds onto itself, forming VGAM1798 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60016] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1798 folded precursor RNA into VGAM1798 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1798 RNA is designated SEQ ID:4509, and is provided hereinbelow with reference to the sequence listing part.

[60017] VGAM1798 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1798 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1798 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60018] VGAM1798 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1798 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1798 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1798 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1798 host target RNA,



herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[60019] The complementary binding of VGAM1798 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1798 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1798 host target RNA into VGAM1798 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60020] It is appreciated that VGAM1798 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1798 host target genes. The mRNA of each one of this plurality of VGAM1798 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1798 RNA, herein designated VGAM RNA, and which when bound by VGAM1798 RNA causes inhibition of translation of respective one or more

VGAM1798 host target proteins.

[60021] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1798 gene, herein designated VGAM GENE, on one or more VGAM1798 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60022] It is yet further appreciated that a function of VGAM1798 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1798 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus.

Specific functions, and accordingly utilities, of VGAM1798 correlate with, and may be deduced from, the identity of the host target genes which VGAM1798 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60023] Nucleotide sequences of the VGAM1798 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1798 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1798 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1798 are further described hereinbelow with reference to Table 1.

[60024] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1798 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1798 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60025] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1798 gene, herein designated VGAM is inhibition of expression of VGAM1798 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1798 correlate with, and may be deduced from, the identity of the target genes which VGAM1798 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60026] Synaptosomal-associated Protein, 25kDa (SNAP25, Accession NM\_003081) is a VGAM1798 host target gene.

SNAP25 BINDING SITE1 and SNAP25 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SNAP25, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAP25 BINDING SITE1 and SNAP25 BINDING SITE2, designated SEQ ID:9054 and SEQ ID:28317 respectively, to the nucleotide sequence of VGAM1798 RNA, herein designated VGAM RNA, also designated SEQ ID:4509.

[60027] A function of VGAM1798 is therefore inhibition of Synaptosomal-associated Protein, 25kDa (SNAP25, Accession NM\_003081). Accordingly, utilities of VGAM1798 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAP25. LOC158332 (Accession XM\_088554) is another VGAM1798 host target gene. LOC158332 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by LOC158332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158332 BINDING SITE, designated SEQ ID:39823, to the nucleotide sequence of VGAM1798 RNA, herein designated VGAM RNA, also designated SEQ ID:4509.

[60028] Another function of VGAM1798 is therefore inhibition of LOC158332 (Accession XM\_088554). Accordingly, utilities of VGAM1798 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158332. LOC84549 (Accession NM\_032509) is another VGAM1798 host target gene. LOC84549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC84549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC84549 BINDING SITE, designated SEQ ID:26259, to the nucleotide sequence of VGAM1798 RNA, herein designated VGAM RNA, also designated SEQ ID:4509.

[60029] Another function of VGAM1798 is therefore inhibition of

LOC84549 (Accession NM\_032509). Accordingly, utilities of VGAM1798 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC84549. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1799 (VGAM1799) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60030] VGAM1799 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1799 was detected is described hereinabove with reference to Figs. 1-8.

[60031] VGAM1799 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1799 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60032] VGAM1799 gene encodes a VGAM1799 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1799 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1799 precursor RNA is designated SEQ ID:1785, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1785 is located at position 30160 relative to the genome of Tupaia Herpesvirus.

- [60033] VGAM1799 precursor RNA folds onto itself, forming VGAM1799 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [60034] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1799 folded precursor RNA into VGAM1799 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide se-

quence of VGAM1799 RNA is designated SEQ ID:4510, and is provided hereinbelow with reference to the sequence listing part.

[60035] VGAM1799 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1799 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1799 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60036] VGAM1799 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1799 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1799 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is



meant as an illustration only, and is not meant to be limiting – VGAM1799 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1799 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[60037] The complementary binding of VGAM1799 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1799 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1799 host target RNA into VGAM1799 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60038] It is appreciated that VGAM1799 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1799 host target genes. The mRNA of each one of this plurality of VGAM1799 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1799 RNA, herein designated VGAM RNA, and which when bound by VGAM1799 RNA causes inhibition of translation of respective one or more VGAM1799 host target proteins.

[60039] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1799 gene, herein designated VGAM GENE, on one or more VGAM1799 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60040] It is yet further appreciated that a function of VGAM1799

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1799 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1799 correlate with, and may be deduced from, the identity of the host target genes which VGAM1799 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60041] Nucleotide sequences of the VGAM1799 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1799 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1799 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1799 are further described hereinbelow with reference to Table 1.

[60042] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1799 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1799 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60043] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1799 gene, herein designated VGAM is inhibition of expression of VGAM1799 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1799 correlate with, and may be deduced from, the identity of the target genes which VGAM1799 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60044] Cyclin F (CCNF, Accession NM\_001761) is a VGAM1799 host target gene. CCNF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCNF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNF BINDING SITE, designated SEQ ID:7523, to the nucleotide sequence of VGAM1799 RNA, herein designated VGAM RNA, also designated SEQ ID:4510.

[60045] A function of VGAM1799 is therefore inhibition of Cyclin F (CCNF, Accession NM\_001761), a gene which likely to be involved in the control of the cell cycle during S phase and G2. Accordingly, utilities of VGAM1799 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with CCNF. The function of CCNF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM367.LOC200574 (Accession XM\_114264) is another VGAM1799 host target gene. LOC200574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200574 BINDING SITE, designated SEQ ID:42821, to the nucleotide sequence of VGAM1799 RNA, herein designated VGAM RNA, also designated SEQ ID:4510.

[60046] Another function of VGAM1799 is therefore inhibition of LOC200574 (Accession XM\_114264). Accordingly, utilities of VGAM1799 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200574. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1800 (VGAM1800) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[60047] VGAM1800 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1800 was detected is described hereinabove with reference to Figs. 1–8.

[60048] VGAM1800 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1800 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60049] VGAM1800 gene encodes a VGAM1800 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1800 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1800 precursor RNA is designated SEQ ID:1786, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1786 is located at position 23754 relative to the genome of Tupaia Herpesvirus.

[60050] VGAM1800 precursor RNA folds onto itself, forming VGAM1800 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60051] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1800 folded precursor RNA into VGAM1800 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1800 RNA is designated SEQ ID:4511, and is provided hereinbelow with reference to the sequence listing part.

[60052] VGAM1800 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1800 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1800 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60053] VGAM1800 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1800 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1800 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1800 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1800 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in



the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60054] The complementary binding of VGAM1800 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1800 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1800 host target RNA into VGAM1800 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60055] It is appreciated that VGAM1800 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1800 host target genes. The mRNA of each one of this plurality of VGAM1800 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1800 RNA, herein designated VGAM RNA, and which when bound by VGAM1800 RNA causes inhibition of translation of respective one or more VGAM1800 host target proteins.

[60056] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1800 gene, herein designated VGAM GENE, on one or more VGAM1800 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60057] It is yet further appreciated that a function of VGAM1800 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1800 correlate with, and may be deduced from, the identity of the host target genes which VGAM1800 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[60058] Nucleotide sequences of the VGAM1800 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1800 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1800 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1800 are further described hereinbelow with reference to Table 1.

[60059] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1800 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1800 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60060] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1800 gene, herein designated VGAM is inhibition of expression of VGAM1800 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1800 correlate with, and may be deduced from, the identity of the target genes which VGAM1800 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60061] Cyclin D2 (CCND2, Accession NM\_001759) is a VGAM1800 host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7516, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60062] A function of VGAM1800 is therefore inhibition of Cyclin D2 (CCND2, Accession NM\_001759), a gene which is essential for the control of the cell cycle at the G1/S (start) transition. Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128. Cytochrome P450, Subfamily IVA, Polypeptide 11 (CYP4A11, Accession NM\_000778) is another VGAM1800 host target gene. CYP4A11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by CYP4A11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP4A11 BINDING SITE, designated SEQ ID:6418, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60063] Another function of VGAM1800 is therefore inhibition of Cytochrome P450, Subfamily IVA, Polypeptide 11 (CYP4A11, Accession NM\_000778), a gene which catalyzes the omega- and (omega-1)-hydroxylation of various fatty acids . Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP4A11. The function of CYP4A11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM798. Leukocyte Immunoglobulin-like Receptor, Subfamily B (with TM and ITIM domains), Member 1 (LILRB1, Accession NM\_006669) is another VGAM1800 host target gene. LILRB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LILRB1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LILRB1 BINDING SITE, designated SEQ ID:13485, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60064] Another function of VGAM1800 is therefore inhibition of Leukocyte Immunoglobulin-like Receptor, Subfamily B (with TM and ITIM domains), Member 1 (LILRB1, Accession NM\_006669). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LILRB1. Vitamin D (1,25-dihydroxyvitamin D3) Receptor (VDR, Accession NM\_000376) is another VGAM1800 host target gene. VDR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VDR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VDR BINDING SITE, designated SEQ ID:5943, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60065] Another function of VGAM1800 is therefore inhibition of

Vitamin D (1,25– dihydroxyvitamin D3) Receptor (VDR, Accession NM\_000376). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VDR. Zinc Finger Protein 217 (ZNF217, Accession NM\_006526) is another VGAM1800 host target gene. ZNF217 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF217, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF217 BINDING SITE, designated SEQ ID:13278, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60066] Another function of VGAM1800 is therefore inhibition of Zinc Finger Protein 217 (ZNF217, Accession NM\_006526). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF217. ATPase, Class V, Type 10B (ATP10B, Accession XM\_032721) is another VGAM1800 host target gene. ATP10B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATP10B, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP10B BINDING SITE, designated SEQ ID:31733, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60067] Another function of VGAM1800 is therefore inhibition of ATPase, Class V, Type 10B (ATP10B, Accession XM\_032721). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP10B. FLJ10246 (Accession NM\_018038) is another VGAM1800 host target gene. FLJ10246 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10246, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10246 BINDING SITE, designated SEQ ID:19784, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60068] Another function of VGAM1800 is therefore inhibition of FLJ10246 (Accession NM\_018038). Accordingly, utilities of



VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10246. KIAA0532 (Accession XM\_047659) is another VGAM1800 host target gene. KIAA0532 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0532 BINDING SITE, designated SEQ ID:35021, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60069] Another function of VGAM1800 is therefore inhibition of KIAA0532 (Accession XM\_047659). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0532. LAK-4P (Accession NM\_007267) is another VGAM1800 host target gene. LAK-4P BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LAK-4P, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAK-4P

BINDING SITE, designated SEQ ID:14132, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60070] Another function of VGAM1800 is therefore inhibition of LAK-4P (Accession NM\_007267). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAK-4P. LOC146517 (Accession XM\_085491) is another VGAM1800 host target gene. LOC146517 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146517, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146517 BINDING SITE, designated SEQ ID:38182, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60071] Another function of VGAM1800 is therefore inhibition of LOC146517 (Accession XM\_085491). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146517. LOC149842 (Accession XM\_097745) is another VGAM1800 host target gene. LOC149842 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149842 BINDING SITE, designated SEQ ID:41089, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60072] Another function of VGAM1800 is therefore inhibition of LOC149842 (Accession XM\_097745). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149842. LOC254243 (Accession XM\_173233) is another VGAM1800 host target gene. LOC254243 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254243 BINDING SITE, designated SEQ ID:46513, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60073] Another function of VGAM1800 is therefore inhibition of

LOC254243 (Accession XM\_173233). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254243. LOC254413 (Accession XM\_173141) is another VGAM1800 host target gene. LOC254413 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254413 BINDING SITE, designated SEQ ID:46402, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60074] Another function of VGAM1800 is therefore inhibition of LOC254413 (Accession XM\_173141). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254413. LOC90038 (Accession XM\_028305) is another VGAM1800 host target gene. LOC90038 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC90038 BINDING SITE, designated SEQ ID:30650, to the nucleotide sequence of VGAM1800 RNA, herein designated VGAM RNA, also designated SEQ ID:4511.

[60075] Another function of VGAM1800 is therefore inhibition of LOC90038 (Accession XM\_028305). Accordingly, utilities of VGAM1800 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90038. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1801 (VGAM1801) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60076] VGAM1801 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1801 was detected is described hereinabove with reference to Figs. 1–8.

[60077] VGAM1801 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1801 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[60078] VGAM1801 gene encodes a VGAM1801 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1801 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1801 precursor RNA is designated SEQ ID:1787, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1787 is located at position 28609 relative to the genome of Tupaia Herpesvirus.

[60079] VGAM1801 precursor RNA folds onto itself, forming VGAM1801 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60080] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1801 folded precursor RNA into VGAM1801 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1801 RNA is designated SEQ ID:4512, and is provided hereinbelow with reference to the sequence listing part.

[60081] VGAM1801 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1801 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1801 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60082] VGAM1801 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1801 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1801 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1801 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1801 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60083] The complementary binding of VGAM1801 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1801 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1801 host target RNA into VGAM1801 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[60084] It is appreciated that VGAM1801 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1801 host target genes. The mRNA of each one of this plurality of VGAM1801 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1801 RNA, herein designated VGAM RNA, and which when bound by VGAM1801 RNA causes inhibition of translation of respective one or more VGAM1801 host target proteins.

[60085] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1801 gene, herein designated VGAM GENE, on one or more VGAM1801 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60086] It is yet further appreciated that a function of VGAM1801 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1801 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1801 correlate with, and may be deduced from, the identity of the host target genes which VGAM1801 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60087] Nucleotide sequences of the VGAM1801 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1801 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1801 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1801 are further described hereinbelow with reference to Table 1.

[60088] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1801 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1801 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60089] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1801 gene, herein designated VGAM is inhibition of expression of VGAM1801 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1801 correlate with, and may be deduced from, the identity of the target genes which VGAM1801 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60090] COAS3 (Accession NM\_139020) is a VGAM1801 host target gene. COAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COAS3 BINDING SITE, designated SEQ ID:29121, to the nucleotide sequence of VGAM1801 RNA, herein designated VGAM RNA, also designated SEQ ID:4512.

[60091] A function of VGAM1801 is therefore inhibition of COAS3 (Accession NM\_139020). Accordingly, utilities of VGAM1801 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COAS3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1802 (VGAM1802) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60092] VGAM1802 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1802 was detected is described hereinabove with reference to Figs. 1-8.

[60093] VGAM1802 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1802 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60094] VGAM1802 gene encodes a VGAM1802 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1802 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1802 precursor RNA is designated SEQ ID:1788, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1788 is located at position 27372 relative to the genome of Tupaia Herpesvirus.

- [60095] VGAM1802 precursor RNA folds onto itself, forming VGAM1802 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [60096] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1802 folded precursor RNA into VGAM1802 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide se-

quence of VGAM1802 RNA is designated SEQ ID:4513, and is provided hereinbelow with reference to the sequence listing part.

[60097] VGAM1802 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1802 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1802 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60098] VGAM1802 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1802 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1802 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1802 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1802 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[60099] The complementary binding of VGAM1802 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1802 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1802 host target RNA into VGAM1802 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60100] It is appreciated that VGAM1802 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1802 host target genes. The mRNA of each one of this plurality of VGAM1802 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1802 RNA, herein designated VGAM RNA, and which when bound by VGAM1802 RNA causes inhibition of translation of respective one or more VGAM1802 host target proteins.

[60101] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1802 gene, herein designated VGAM GENE, on one or more VGAM1802 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60102] It is yet further appreciated that a function of VGAM1802



is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1802 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1802 correlate with, and may be deduced from, the identity of the host target genes which VGAM1802 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60103] Nucleotide sequences of the VGAM1802 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1802 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1802 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1802 are further described hereinbelow with reference to Table 1.

[60104] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1802 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1802 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60105] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1802 gene, herein designated VGAM is inhibition of expression of VGAM1802 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1802 correlate with, and may be deduced from, the identity of the target genes which VGAM1802 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60106] MGC11061 (Accession NM\_032312) is a VGAM1802 host target gene. MGC11061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11061 BINDING SITE, designated SEQ ID:26115, to the nucleotide sequence of VGAM1802 RNA, herein designated VGAM RNA, also designated SEQ ID:4513.

[60107] A function of VGAM1802 is therefore inhibition of MGC11061 (Accession NM\_032312). Accordingly, utilities of VGAM1802 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11061. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1803 (VGAM1803) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60108] VGAM1803 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1803 was detected is described hereinabove with reference to Figs. 1–8.

[60109] VGAM1803 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1803 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60110] VGAM1803 gene encodes a VGAM1803 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1803 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1803 precursor RNA is designated SEQ ID:1789, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1789 is located at position 29560 relative to the genome of Tupaia Herpesvirus.

[60111] VGAM1803 precursor RNA folds onto itself, forming VGAM1803 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60112] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1803 folded precursor RNA into VGAM1803 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1803 RNA is designated SEQ ID:4514, and is provided hereinbelow with reference to the sequence listing part.

[60113] VGAM1803 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1803 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1803 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60114] VGAM1803 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1803 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1803 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1803 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1803 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[60115] The complementary binding of VGAM1803 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1803 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1803 host target RNA into VGAM1803 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60116] It is appreciated that VGAM1803 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1803 host target genes. The mRNA of each one of this plurality of VGAM1803 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1803 RNA, herein designated VGAM RNA, and which when bound by VGAM1803 RNA causes inhibition of translation of respective one or more

VGAM1803 host target proteins.

[60117] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1803 gene, herein designated VGAM GENE, on one or more VGAM1803 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60118] It is yet further appreciated that a function of VGAM1803 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1803 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific

functions, and accordingly utilities, of VGAM1803 correlate with, and may be deduced from, the identity of the host target genes which VGAM1803 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60119] Nucleotide sequences of the VGAM1803 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1803 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1803 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1803 are further described hereinbelow with reference to Table 1.

[60120] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1803 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1803 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60121] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1803 gene, herein designated VGAM is inhibition of expression of VGAM1803 target genes. It is appreciated that specific functions, and accordingly utili-



ties, of VGAM1803 correlate with, and may be deduced from, the identity of the target genes which VGAM1803 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60122] Chromosome 20 Open Reading Frame 177 (C20orf177, Accession XM\_030726) is a VGAM1803 host target gene. C20orf177 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf177 BINDING SITE, designated SEQ ID:31128, to the nucleotide sequence of VGAM1803 RNA, herein designated VGAM RNA, also designated SEQ ID:4514.

[60123] A function of VGAM1803 is therefore inhibition of Chromosome 20 Open Reading Frame 177 (C20orf177, Accession XM\_030726). Accordingly, utilities of VGAM1803 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf177. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1804

(VGAM1804) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60124] VGAM1804 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1804 was detected is described hereinabove with reference to Figs. 1–8.

[60125] VGAM1804 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1804 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60126] VGAM1804 gene encodes a VGAM1804 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1804 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1804 precursor RNA is designated SEQ ID:1790, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1790 is located at position 30515 relative to the genome of Tupaia Herpesvirus.

[60127] VGAM1804 precursor RNA folds onto itself, forming

VGAM1804 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60128] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1804 folded precursor RNA into VGAM1804 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1804 RNA is designated SEQ ID:4515, and is provided hereinbelow with reference to the sequence listing part.

[60129] VGAM1804 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1804 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1804 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60130] VGAM1804 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1804 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1804 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1804 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1804 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60131] The complementary binding of VGAM1804 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1804 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1804 host target RNA into VGAM1804 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60132] It is appreciated that VGAM1804 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1804 host target genes. The mRNA of each one of this plurality of VGAM1804 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1804 RNA, herein designated VGAM RNA, and which when bound by VGAM1804 RNA causes inhibition of translation of respective one or more VGAM1804 host target proteins.

[60133] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1804 gene, herein designated VGAM GENE, on one or more VGAM1804 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60134] It is yet further appreciated that a function of VGAM1804 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1804 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1804 correlate with, and may be deduced from, the identity of the host target genes which VGAM1804 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[60135] Nucleotide sequences of the VGAM1804 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1804 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1804 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1804 are further described hereinbelow with reference to Table 1.

[60136] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1804 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1804 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60137] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1804 gene, herein designated VGAM is inhibition of expression of VGAM1804 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1804 correlate with, and may be deduced from, the identity of the target genes which VGAM1804 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60138] Chemokine (C-C motif) Receptor 2 (CCR2, Accession NM\_000647) is a VGAM1804 host target gene. CCR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR2 BINDING SITE, designated SEQ ID:6310, to the nucleotide sequence of VGAM1804 RNA, herein designated VGAM RNA, also designated SEQ ID:4515.

[60139] A function of VGAM1804 is therefore inhibition of Chemokine (C-C motif) Receptor 2 (CCR2, Accession NM\_000647), a gene which binds chemokines and transduces a signal by increasing the intracellular calcium ions level. Accordingly, utilities of VGAM1804 include diagno-



sis, prevention and treatment of diseases and clinical conditions associated with CCR2. The function of CCR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM206. Mannose-binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM\_000242) is another VGAM1804 host target gene. MBL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBL2 BINDING SITE, designated SEQ ID:5764, to the nucleotide sequence of VGAM1804 RNA, herein designated VGAM RNA, also designated SEQ ID:4515.

[60140] Another function of VGAM1804 is therefore inhibition of Mannose-binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM\_000242). Accordingly, utilities of VGAM1804 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBL2. PDGFA Associated Protein 1 (PDAP1, Accession XM\_166484) is another VGAM1804 host target gene.

PDAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDAP1 BINDING SITE, designated SEQ ID:44419, to the nucleotide sequence of VGAM1804 RNA, herein designated VGAM RNA, also designated SEQ ID:4515.

[60141] Another function of VGAM1804 is therefore inhibition of PDGFA Associated Protein 1 (PDAP1, Accession XM\_166484). Accordingly, utilities of VGAM1804 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDAP1. KIAA1668 (Accession XM\_039236) is another VGAM1804 host target gene. KIAA1668 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1668 BINDING SITE, designated SEQ ID:33026, to the nucleotide sequence of VGAM1804 RNA, herein designated VGAM RNA, also designated SEQ

ID:4515.

[60142] Another function of VGAM1804 is therefore inhibition of KIAA1668 (Accession XM\_039236). Accordingly, utilities of VGAM1804 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1668. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1805 (VGAM1805) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60143] VGAM1805 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1805 was detected is described hereinabove with reference to Figs. 1–8.

[60144] VGAM1805 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1805 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60145] VGAM1805 gene encodes a VGAM1805 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1805 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1805 precursor RNA is designated SEQ ID:1791, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1791 is located at position 33339 relative to the genome of Tupaia Herpesvirus.

[60146] VGAM1805 precursor RNA folds onto itself, forming VGAM1805 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60147] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1805 folded precursor RNA into VGAM1805 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1805 RNA is designated SEQ ID:4516, and is provided hereinbelow with reference to the sequence listing part.

[60148] VGAM1805 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1805 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1805 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60149] VGAM1805 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1805 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1805 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1805 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1805 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[60150] The complementary binding of VGAM1805 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1805 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1805 host target RNA into VGAM1805 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60151] It is appreciated that VGAM1805 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1805 host target genes. The mRNA of

each one of this plurality of VGAM1805 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1805 RNA, herein designated VGAM RNA, and which when bound by VGAM1805 RNA causes inhibition of translation of respective one or more VGAM1805 host target proteins.

[60152] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1805 gene, herein designated VGAM GENE, on one or more VGAM1805 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[60153] It is yet further appreciated that a function of VGAM1805 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1805 correlate with, and may be deduced from, the identity of the host target genes which VGAM1805 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60154] Nucleotide sequences of the VGAM1805 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1805 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1805 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1805 are further described hereinbelow with reference to Table 1.

[60155] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1805 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1805 RNA,



herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60156] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1805 gene, herein designated VGAM is inhibition of expression of VGAM1805 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1805 correlate with, and may be deduced from, the identity of the target genes which VGAM1805 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60157] Alcohol Dehydrogenase IB (class I), Beta Polypeptide (ADH1B, Accession XM\_052365) is a VGAM1805 host target gene. ADH1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADH1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADH1B BINDING SITE, designated SEQ ID:35960, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60158] A function of VGAM1805 is therefore inhibition of Alcohol Dehydrogenase IB (class I), Beta Polypeptide (ADH1B, Ac-

cession XM\_052365), a gene which Alcohol dehydrogenase 2 (alcohol:NAD<sup>+</sup> oxidoreductase) class I beta subunit. Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADH1B. The function of ADH1B has been established by previous studies. See 103700 for evidence on the mapping of the ADH2 gene in the cluster of related genes on 4q22. According to the conclusion of Smith et al. (1973), locus ADH2 is expressed in the lung in early fetal life and remains active in this tissue throughout life. It is active also in liver after about the first trimester and gradually increases in activity so that in adults this locus is responsible for most of the liver ADH activity. It is active in the adult kidney. The 'atypical pH ratio' phenotype is probably determined by a variant allele at the ADH2 locus. Stamatoyannopoulos et al. (1975) found that 85% of Japanese carry an atypical liver ADH (ADH2 type). About the same proportion have alcohol sensitivity, which they suggest may be due to increased formation of acetaldehyde by persons with the atypical ADH. Bosron et al. (1980) found new molecular forms of human ADH, collectively designated ADH(Indianapolis), in 29% of liver specimens from black Americans. Three different Indianapolis

ADH phenotypes were identified by starch gel electrophoresis and 4 isolated by affinity and ion-exchange chromatography. One is a homodimer of a newly discovered subunit. The other 3 are heterodimers of this new subunit and the known subunits, alpha, beta-1, and gamma-1. Agarwal et al. (1981) could find no instance of the Indianapolis variant in Germany or Japan; it may be confined to American blacks. Bosron et al. (1983) concluded that the Indianapolis phenotypes reflect polymorphism at the ADH2 locus with the variant ADH(Indianapolis) allele coding for the beta-Indianapolis subunit. The frequency of this allele was 0.16 in black Americans and was not found in any of 63 livers from white Americans. The frequency of alleles at the ADH3 locus also differs in these 2 populations. Two of the 3 class I genes (ADHB and ADHC) are known to have alleles that produce enzymes that catalyze the oxidation of ethanol at different rates. At the protein level, the allelic series for ADH1B is generated by variation at 2 different sites at the genomic level: the ADH1B\*1 allele is composed of 47arg and 369arg, the ADH1B\*2 allele is composed of 47his and 369arg (see OMIM Ref. No. 103720.0001), and the ADH1B\*3 allele (103720.0002) is composed of 47arg and

369cys. Osier et al. (2002) stated that the 'double variant' (composed of 47his and 369cys) could exist but had not been observed.

[60159] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[60160] Bosron, W. F.; Magnes, L. J.; Li, T.-K. : Human liver alcohol dehydrogenase: ADH(Indianapolis) results from genetic polymorphism at the ADH-2 gene locus. Biochem. Genet. 21: 735-744, 1983. ; and

[60161] Osier, M. V.; Pakstis, A. J.; Soodyall, H.; Comas, D.; Goldman, D.; Odunsi, A.; Okonofua, F.; Parnas, J.; Schulz, L. O.; Bertranpetit, J.; Bonne-Tamir, B.; Lu, R.-B.; Kidd, J. R.; Kidd.

[60162] Further studies establishing the function and utilities of ADH1B are found in John Hopkins OMIM database record ID 103720, and in cited publications numbered 819-822, 4161, 12101-829, 12096, 12102, 378 and 12103-503 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 1; Cyclin D-related (CBFA2T1, Accession NM\_004349) is another VGAM1805 host target gene. CBFA2T1 BINDING SITE

is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFA2T1 BINDING SITE, designated SEQ ID:10542, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60163] Another function of VGAM1805 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 1; Cyclin D-related (CBFA2T1, Accession NM\_004349), a gene which produces a chimeric gene made up of the 5-prime region of the AML1 gene fused to the 3-prime region of the ETO gene through translocation. Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T1. The function of CBFA2T1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM113. Doublesex and Mab-3 Related Transcription Factor 1 (DMRT1, Accession NM\_021951) is another VGAM1805 host target gene. DMRT1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DMRT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMRT1 BINDING SITE, designated SEQ ID:22480, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60164] Another function of VGAM1805 is therefore inhibition of Doublesex and Mab-3 Related Transcription Factor 1 (DMRT1, Accession NM\_021951), a gene which May be involved in male sexual development. Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMRT1. The function of DMRT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM59. Early Growth Response 3 (EGR3, Accession XM\_005040) is another VGAM1805 host target gene. EGR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of EGR3 BINDING SITE, designated SEQ ID:29961, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60165] Another function of VGAM1805 is therefore inhibition of Early Growth Response 3 (EGR3, Accession XM\_005040), a gene which is a putative transcription factor. Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGR3. The function of EGR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM189. Mesenchyme Homeo Box 2 (growth arrest-specific homeo box) (MEOX2, Accession NM\_005924) is another VGAM1805 host target gene. MEOX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEOX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEOX2 BINDING SITE, designated SEQ ID:12552, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ

ID:4516.

[60166] Another function of VGAM1805 is therefore inhibition of Mesenchyme Homeo Box 2 (growth arrest-specific homeo box) (MEOX2, Accession NM\_005924), a gene which roles in mesoderm induction and, somitogenesis, and myogenic and sclerotomal differentiation. Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEOX2. The function of MEOX2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827. Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, Drosophila) (PDE4D, Accession XM\_056815) is another VGAM1805 host target gene. PDE4D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4D BINDING SITE, designated SEQ ID:36436, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.



[60167] Another function of VGAM1805 is therefore inhibition of Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, *Drosophila*) (PDE4D, Accession XM\_056815), a gene which has similarity to *Drosophila* dnc, which is the affected protein in learning and memory mutant dunce. Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4D. The function of PDE4D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Pleiomorphic Adenoma Gene 1 (PLAG1, Accession NM\_002655) is another VGAM1805 host target gene. PLAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAG1 BINDING SITE, designated SEQ ID:8518, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60168] Another function of VGAM1805 is therefore inhibition of Pleiomorphic Adenoma Gene 1 (PLAG1, Accession

NM\_002655), a gene which contains a zinc finger domain. Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAG1. The function of PLAG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM29. Protein Tyrosine Phosphatase Type IVA, Member 2 (PTP4A2, Accession NM\_003479) is another VGAM1805 host target gene. PTP4A2 BINDING SITE1 and PTP4A2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTP4A2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTP4A2 BINDING SITE1 and PTP4A2 BINDING SITE2, designated SEQ ID:9549 and SEQ ID:27829 respectively, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60169] Another function of VGAM1805 is therefore inhibition of Protein Tyrosine Phosphatase Type IVA, Member 2 (PTP4A2, Accession NM\_003479), a gene which is a protein tyrosine phosphatase which has a C-terminal preny-

lation site. Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTP4A2. The function of PTP4A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. TRAM (Accession NM\_014294) is another VGAM1805 host target gene. TRAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAM BINDING SITE, designated SEQ ID:15590, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60170] Another function of VGAM1805 is therefore inhibition of TRAM (Accession NM\_014294). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAM. CCR4-NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM\_004779) is another VGAM1805 host target gene. CNOT8 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by CNOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT8 BINDING SITE, designated SEQ ID:11181, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60171] Another function of VGAM1805 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM\_004779). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT8. FYVE and Coiled–coil Domain Containing 1 (FYCO1, Accession NM\_024513) is another VGAM1805 host target gene. FYCO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FYCO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FYCO1 BINDING SITE, designated SEQ ID:23713, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ

ID:4516.

[60172] Another function of VGAM1805 is therefore inhibition of FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM\_024513). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FYCO1. Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 1 (KCNS1, Accession NM\_002251) is another VGAM1805 host target gene. KCNS1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNS1 BINDING SITE, designated SEQ ID:8041, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60173] Another function of VGAM1805 is therefore inhibition of Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 1 (KCNS1, Accession NM\_002251). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNS1. KIAA1237 (Accession XM\_087386)

is another VGAM1805 host target gene. KIAA1237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1237 BINDING SITE, designated SEQ ID:39221, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60174] Another function of VGAM1805 is therefore inhibition of KIAA1237 (Accession XM\_087386). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1237. KIAA1254 (Accession XM\_046132) is another VGAM1805 host target gene. KIAA1254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1254 BINDING SITE, designated SEQ ID:34696, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60175] Another function of VGAM1805 is therefore inhibition of KIAA1254 (Accession XM\_046132). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1254. KIAA1287 (Accession XM\_085753) is another VGAM1805 host target gene. KIAA1287 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1287, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1287 BINDING SITE, designated SEQ ID:38325, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60176] Another function of VGAM1805 is therefore inhibition of KIAA1287 (Accession XM\_085753). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1287. MGC14161 (Accession NM\_032892) is another VGAM1805 host target gene. MGC14161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC14161, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14161 BINDING SITE, designated SEQ ID:26717, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60177] Another function of VGAM1805 is therefore inhibition of MGC14161 (Accession NM\_032892). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14161. MGC33182 (Accession XM\_062903) is another VGAM1805 host target gene. MGC33182 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC33182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC33182 BINDING SITE, designated SEQ ID:37234, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60178] Another function of VGAM1805 is therefore inhibition of MGC33182 (Accession XM\_062903). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



MGC33182. PRO1992 (Accession NM\_014107) is another VGAM1805 host target gene. PRO1992 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1992 BINDING SITE, designated SEQ ID:15331, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60179] Another function of VGAM1805 is therefore inhibition of PRO1992 (Accession NM\_014107). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1992. RABEX5 (Accession NM\_014504) is another VGAM1805 host target gene. RABEX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RABEX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RABEX5 BINDING SITE, designated SEQ ID:15839, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM

RNA, also designated SEQ ID:4516.

[60180] Another function of VGAM1805 is therefore inhibition of RABEX5 (Accession NM\_014504). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RABEX5. LOC118611 (Accession XM\_061055) is another VGAM1805 host target gene. LOC118611 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC118611, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118611 BINDING SITE, designated SEQ ID:37189, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60181] Another function of VGAM1805 is therefore inhibition of LOC118611 (Accession XM\_061055). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118611. LOC152715 (Accession XM\_087511) is another VGAM1805 host target gene. LOC152715 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC152715, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152715 BINDING SITE, designated SEQ ID:39303, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60182] Another function of VGAM1805 is therefore inhibition of LOC152715 (Accession XM\_087511). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152715. LOC220143 (Accession XM\_168046) is another VGAM1805 host target gene. LOC220143 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220143 BINDING SITE, designated SEQ ID:44956, to the nucleotide sequence of VGAM1805 RNA, herein designated VGAM RNA, also designated SEQ ID:4516.

[60183] Another function of VGAM1805 is therefore inhibition of LOC220143 (Accession XM\_168046). Accordingly, utilities of VGAM1805 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC220143. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1806 (VGAM1806) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60184] VGAM1806 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1806 was detected is described hereinabove with reference to Figs. 1–8.

[60185] VGAM1806 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1806 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60186] VGAM1806 gene encodes a VGAM1806 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1806 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1806 precursor RNA is desig-

nated SEQ ID:1792, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1792 is located at position 25245 relative to the genome of Tupaia Herpesvirus.

- [60187] VGAM1806 precursor RNA folds onto itself, forming VGAM1806 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [60188] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1806 folded precursor RNA into VGAM1806 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1806 RNA is designated SEQ ID:4517, and is provided hereinbelow with reference to the sequence

listing part.

[60189] VGAM1806 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1806 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1806 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60190] VGAM1806 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1806 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1806 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1806 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1806 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60191] The complementary binding of VGAM1806 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1806 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1806 host target RNA into VGAM1806 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60192] It is appreciated that VGAM1806 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1806 host target genes. The mRNA of each one of this plurality of VGAM1806 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1806 RNA, herein designated VGAM

RNA, and which when bound by VGAM1806 RNA causes inhibition of translation of respective one or more VGAM1806 host target proteins.

[60193] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1806 gene, herein designated VGAM GENE, on one or more VGAM1806 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60194] It is yet further appreciated that a function of VGAM1806 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,



utilities of VGAM1806 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1806 correlate with, and may be deduced from, the identity of the host target genes which VGAM1806 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60195] Nucleotide sequences of the VGAM1806 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1806 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1806 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1806 are further described hereinbelow with reference to Table 1.

[60196] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1806 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1806 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60197] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1806 gene, herein designated VGAM is

inhibition of expression of VGAM1806 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1806 correlate with, and may be deduced from, the identity of the target genes which VGAM1806 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60198] Carbohydrate Kinase-like (CARKL, Accession NM\_013276) is a VGAM1806 host target gene. CARKL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARKL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARKL BINDING SITE, designated SEQ ID:14941, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60199] A function of VGAM1806 is therefore inhibition of Carbohydrate Kinase-like (CARKL, Accession NM\_013276), a gene which is a putative carbohydrate kinase and may be a modifier for the cystinosis phenotype. Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARKL. The function of CARKL and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM419.PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM\_015866) is another VGAM1806 host target gene. PRDM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRDM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM2 BINDING SITE, designated SEQ ID:18008, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60200] Another function of VGAM1806 is therefore inhibition of PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM\_015866), a gene which plays a role in transcriptional regulation during neuronal differentiation and pathogenesis of retinoblastoma. Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM2. The function of PRDM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM120.RAB18, Member RAS Oncogene Family (RAB18, Accession NM\_021252) is another VGAM1806 host target gene. RAB18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB18 BINDING SITE, designated SEQ ID:22223, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60201] Another function of VGAM1806 is therefore inhibition of RAB18, Member RAS Oncogene Family (RAB18, Accession NM\_021252), a gene which plays a role in apical endocytosis/recycling. Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB18. The function of RAB18 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120.Tumor Necrosis Factor Receptor Superfamily, Member 11a, Activator of NFkB (TNFRSF11A, Accession NM\_003839) is another VGAM1806 host target gene. TN-

FRSF11A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF11A BINDING SITE, designated SEQ ID:9931, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60202] Another function of VGAM1806 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 11a, Activator of NFkB (TNFRSF11A, Accession NM\_003839). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF11A. Zinc Finger Protein 192 (ZNF192, Accession NM\_006298) is another VGAM1806 host target gene. ZNF192 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF192, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF192 BINDING SITE, designated SEQ ID:12992, to the nucleotide

sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60203] Another function of VGAM1806 is therefore inhibition of Zinc Finger Protein 192 (ZNF192, Accession NM\_006298). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF192. Adaptor-related Protein Complex 3, Delta 1 Subunit (AP3D1, Accession NM\_003938) is another VGAM1806 host target gene. AP3D1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP3D1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP3D1 BINDING SITE, designated SEQ ID:10048, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60204] Another function of VGAM1806 is therefore inhibition of Adaptor-related Protein Complex 3, Delta 1 Subunit (AP3D1, Accession NM\_003938). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP3D1.

CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM\_004779) is another VGAM1806 host target gene. CNOT8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT8 BINDING SITE, designated SEQ ID:11183, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60205] Another function of VGAM1806 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM\_004779). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT8. FLJ10260 (Accession NM\_018042) is another VGAM1806 host target gene. FLJ10260 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10260, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10260 BINDING SITE,

designated SEQ ID:19787, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60206] Another function of VGAM1806 is therefore inhibition of FLJ10260 (Accession NM\_018042). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10260. FLJ12568 (Accession NM\_024993) is another VGAM1806 host target gene. FLJ12568 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12568 BINDING SITE, designated SEQ ID:24553, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60207] Another function of VGAM1806 is therefore inhibition of FLJ12568 (Accession NM\_024993). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12568. Integrin, Beta 5 (ITGB5, Accession XM\_003029) is another VGAM1806 host target gene. ITGB5 BINDING



SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ITGB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGB5 BINDING SITE, designated SEQ ID:29923, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60208] Another function of VGAM1806 is therefore inhibition of Integrin, Beta 5 (ITGB5, Accession XM\_003029). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGB5. KIAA1434 (Accession XM\_045585) is another VGAM1806 host target gene. KIAA1434 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1434 BINDING SITE, designated SEQ ID:34493, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60209] Another function of VGAM1806 is therefore inhibition of

KIAA1434 (Accession XM\_045585). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1434. KIAA1751 (Accession XM\_049768) is another VGAM1806 host target gene. KIAA1751 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1751, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1751 BINDING SITE, designated SEQ ID:35498, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60210] Another function of VGAM1806 is therefore inhibition of KIAA1751 (Accession XM\_049768). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1751. KIAA1854 (Accession XM\_049884) is another VGAM1806 host target gene. KIAA1854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35539, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60211] Another function of VGAM1806 is therefore inhibition of KIAA1854 (Accession XM\_049884). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. MAWBP (Accession NM\_022129) is another VGAM1806 host target gene. MAWBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAWBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAWBP BINDING SITE, designated SEQ ID:22683, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60212] Another function of VGAM1806 is therefore inhibition of MAWBP (Accession NM\_022129). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAWBP. Protein Phosphatase 1A (formerly 2C), Magne-

sium-dependent, Alpha Isoform (PPM1A, Accession NM\_021003) is another VGAM1806 host target gene. PPM1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPM1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPM1A BINDING SITE, designated SEQ ID:22000, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60213] Another function of VGAM1806 is therefore inhibition of Protein Phosphatase 1A (formerly 2C), Magnesium-dependent, Alpha Isoform (PPM1A, Accession NM\_021003). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPM1A. STIP-1 (Accession XM\_045694) is another VGAM1806 host target gene. STIP-1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STIP-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STIP-1 BIND-

ING SITE, designated SEQ ID:34528, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60214] Another function of VGAM1806 is therefore inhibition of STIP-1 (Accession XM\_045694). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STIP-1. TEB4 (Accession XM\_027156) is another VGAM1806 host target gene. TEB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEB4 BINDING SITE, designated SEQ ID:30430, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60215] Another function of VGAM1806 is therefore inhibition of TEB4 (Accession XM\_027156). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEB4. ZW10 Interactor (ZWINT, Accession NM\_032997) is another VGAM1806 host target gene. ZWINT BINDING SITE1

and ZWINT BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ZWINT, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZWINT BINDING SITE1 and ZWINT BINDING SITE2, designated SEQ ID:26876 and SEQ ID:13923 respectively, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60216] Another function of VGAM1806 is therefore inhibition of ZW10 Interactor (ZWINT, Accession NM\_032997). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZWINT. LOC220573 (Accession XM\_045569) is another VGAM1806 host target gene. LOC220573 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220573 BINDING SITE, designated SEQ ID:34485, to the nucleotide sequence of VGAM1806 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4517.

[60217] Another function of VGAM1806 is therefore inhibition of LOC220573 (Accession XM\_045569). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220573. LOC256073 (Accession XM\_172972) is another VGAM1806 host target gene. LOC256073 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256073 BINDING SITE, designated SEQ ID:46230, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60218] Another function of VGAM1806 is therefore inhibition of LOC256073 (Accession XM\_172972). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256073. LOC92606 (Accession XM\_046097) is another VGAM1806 host target gene. LOC92606 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92606, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92606 BINDING SITE, designated SEQ ID:34680, to the nucleotide sequence of VGAM1806 RNA, herein designated VGAM RNA, also designated SEQ ID:4517.

[60219] Another function of VGAM1806 is therefore inhibition of LOC92606 (Accession XM\_046097). Accordingly, utilities of VGAM1806 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92606. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1807 (VGAM1807) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60220] VGAM1807 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1807 was detected is described hereinabove with reference to Figs. 1-8.

[60221] VGAM1807 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus.



VGAM1807 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60222] VGAM1807 gene encodes a VGAM1807 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1807 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1807 precursor RNA is designated SEQ ID:1793, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1793 is located at position 16749 relative to the genome of Rana Tigrina Ranavirus.

[60223] VGAM1807 precursor RNA folds onto itself, forming VGAM1807 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60224] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1807 folded precursor RNA into VGAM1807 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1807 RNA is designated SEQ ID:4518, and is provided hereinbelow with reference to the sequence listing part.

[60225] VGAM1807 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1807 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1807 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60226] VGAM1807 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1807 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1807 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1807 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1807 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60227] The complementary binding of VGAM1807 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1807 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1807 host target RNA into VGAM1807 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60228] It is appreciated that VGAM1807 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1807 host target genes. The mRNA of each one of this plurality of VGAM1807 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1807 RNA, herein designated VGAM RNA, and which when bound by VGAM1807 RNA causes inhibition of translation of respective one or more VGAM1807 host target proteins.

[60229] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1807 gene, herein designated VGAM GENE, on one or more VGAM1807 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60230] It is yet further appreciated that a function of VGAM1807 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1807 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1807 correlate with, and may be deduced from, the identity of the host target genes which VGAM1807 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60231] Nucleotide sequences of the VGAM1807 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1807 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1807 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1807 are further described hereinbelow with reference to Table 1.

[60232] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1807 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1807 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60233] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1807 gene, herein designated VGAM is inhibition of expression of VGAM1807 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1807 correlate with, and may be deduced from, the identity of the target genes which VGAM1807 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60234] KIAA1013 (Accession XM\_114303) is a VGAM1807 host target gene. KIAA1013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1013 BINDING SITE, designated SEQ ID:42860, to the nucleotide sequence of

VGAM1807 RNA, herein designated VGAM RNA, also designated SEQ ID:4518.

[60235] A function of VGAM1807 is therefore inhibition of KIAA1013 (Accession XM\_114303). Accordingly, utilities of VGAM1807 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1013. MGC13007 (Accession NM\_032320) is another VGAM1807 host target gene. MGC13007 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13007 BINDING SITE, designated SEQ ID:26122, to the nucleotide sequence of VGAM1807 RNA, herein designated VGAM RNA, also designated SEQ ID:4518.

[60236] Another function of VGAM1807 is therefore inhibition of MGC13007 (Accession NM\_032320). Accordingly, utilities of VGAM1807 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13007. PTD012 (Accession NM\_014039) is another VGAM1807 host target gene. PTD012 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PTD012, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTD012 BINDING SITE, designated SEQ ID:15269, to the nucleotide sequence of VGAM1807 RNA, herein designated VGAM RNA, also designated SEQ ID:4518.

[60237] Another function of VGAM1807 is therefore inhibition of PTD012 (Accession NM\_014039). Accordingly, utilities of VGAM1807 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTD012. Serum/glucocorticoid Regulated Kinase 2 (SGK2, Accession NM\_016276) is another VGAM1807 host target gene. SGK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SGK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SGK2 BINDING SITE, designated SEQ ID:18399, to the nucleotide sequence of VGAM1807 RNA, herein designated VGAM RNA, also designated SEQ ID:4518.

[60238] Another function of VGAM1807 is therefore inhibition of Serum/glucocorticoid Regulated Kinase 2 (SGK2, Acces-



sion NM\_016276). Accordingly, utilities of VGAM1807 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SGK2. LOC152559 (Accession XM\_087487) is another VGAM1807 host target gene. LOC152559 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152559 BINDING SITE, designated SEQ ID:39286, to the nucleotide sequence of VGAM1807 RNA, herein designated VGAM RNA, also designated SEQ ID:4518.

[60239] Another function of VGAM1807 is therefore inhibition of LOC152559 (Accession XM\_087487). Accordingly, utilities of VGAM1807 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152559. LOC90509 (Accession XM\_032209) is another VGAM1807 host target gene. LOC90509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC90509 BINDING SITE, designated SEQ ID:31609, to the nucleotide sequence of VGAM1807 RNA, herein designated VGAM RNA, also designated SEQ ID:4518.

[60240] Another function of VGAM1807 is therefore inhibition of LOC90509 (Accession XM\_032209). Accordingly, utilities of VGAM1807 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90509. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1808 (VGAM1808) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60241] VGAM1808 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1808 was detected is described hereinabove with reference to Figs. 1–8.

[60242] VGAM1808 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1808 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[60243] VGAM1808 gene encodes a VGAM1808 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1808 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1808 precursor RNA is designated SEQ ID:1794, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1794 is located at position 27725 relative to the genome of Rana Tigrina Ranavirus.

[60244] VGAM1808 precursor RNA folds onto itself, forming VGAM1808 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60245] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1808 folded precursor RNA into VGAM1808 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1808 RNA is designated SEQ ID:4519, and is provided hereinbelow with reference to the sequence listing part.

[60246] VGAM1808 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1808 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1808 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60247] VGAM1808 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1808 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1808 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1808 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1808 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60248] The complementary binding of VGAM1808 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1808 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1808 host target RNA into VGAM1808 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60249] It is appreciated that VGAM1808 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1808 host target genes. The mRNA of each one of this plurality of VGAM1808 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1808 RNA, herein designated VGAM RNA, and which when bound by VGAM1808 RNA causes inhibition of translation of respective one or more VGAM1808 host target proteins.

[60250] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1808 gene, herein designated VGAM GENE, on one or more VGAM1808 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60251] It is yet further appreciated that a function of VGAM1808 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1808 correlate with, and may be deduced from, the identity of the host target genes which VGAM1808 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60252] Nucleotide sequences of the VGAM1808 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1808 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1808 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1808 are further described hereinbelow with reference to Table 1.

[60253] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1808 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1808 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60254] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1808 gene, herein designated VGAM is inhibition of expression of VGAM1808 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1808 correlate with, and may be deduced from, the identity of the target genes which VGAM1808 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60255] Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession NM\_138271) is a VGAM1808 host target gene. ATRX BINDING SITE1 and ATRX BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ATRX, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATRX BINDING SITE1 and ATRX BINDING SITE2, designated SEQ ID:28684 and SEQ ID:6095



respectively, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60256] A function of VGAM1808 is therefore inhibition of Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession NM\_138271). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATRX. Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM\_004021) is another VGAM1808 host target gene. DMD BINDING SITE1 through DMD BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DMD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMD BINDING SITE1 through DMD BINDING SITE3, designated SEQ ID:10224, SEQ ID:10236 and SEQ ID:8261 respectively, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60257] Another function of VGAM1808 is therefore inhibition of Dystrophin (muscular dystrophy, Duchenne and Becker

types) (DMD, Accession NM\_004021), a gene which muscular dystrophy . Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMD. The function of DMD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM218. Prostaglandin F2 Receptor Negative Regulator (PTGFRN, Accession XM\_040709) is another VGAM1808 host target gene. PTGFRN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTGFRN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGFRN BINDING SITE, designated SEQ ID:33362, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60258] Another function of VGAM1808 is therefore inhibition of Prostaglandin F2 Receptor Negative Regulator (PTGFRN, Accession XM\_040709), a gene which inhibits the binding of prostaglandin f2-alpha (pgf2- alpha) to its specific fp receptor. Accordingly, utilities of VGAM1808 include diag-

nosis, prevention and treatment of diseases and clinical conditions associated with PTGFRN. The function of PTGFRN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. Solute Carrier Family 20 (phosphate transporter), Member 1 (SLC20A1, Accession XM\_002217) is another VGAM1808 host target gene. SLC20A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC20A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC20A1 BINDING SITE, designated SEQ ID:29873, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60259] Another function of VGAM1808 is therefore inhibition of Solute Carrier Family 20 (phosphate transporter), Member 1 (SLC20A1, Accession XM\_002217), a gene which could be a sodium-phosphate symporter. Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC20A1. The function of SLC20A1 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM608. Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM\_003043) is another VGAM1808 host target gene. SLC6A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A6 BINDING SITE, designated SEQ ID:9003, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60260] Another function of VGAM1808 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM\_003043), a gene which transports taurine and other beta-amino acids like beta-alanine. Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A6. The function of SLC6A6 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM36. Transient Receptor Potential Cation Channel, Subfamily M, Member 8 (TRPM8, Accession NM\_024080) is another VGAM1808 host target gene. TRPM8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPM8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM8 BINDING SITE, designated SEQ ID:23513, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60261] Another function of VGAM1808 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 8 (TRPM8, Accession NM\_024080), a gene which is thought to form a receptor-activated calcium permeant cation channel. Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM8. The function of TRPM8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM201. Chromosome 20 Open Reading Frame 80

(C20orf80, Accession XM\_037014) is another VGAM1808 host target gene. C20orf80 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf80, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf80 BINDING SITE, designated SEQ ID:32537, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60262] Another function of VGAM1808 is therefore inhibition of Chromosome 20 Open Reading Frame 80 (C20orf80, Accession XM\_037014). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf80. Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM\_032385) is another VGAM1808 host target gene. C5orf4 BINDING SITE1 and C5orf4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by C5orf4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf4 BINDING

SITE1 and C5orf4 BINDING SITE2, designated SEQ ID:26184 and SEQ ID:18476 respectively, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60263] Another function of VGAM1808 is therefore inhibition of Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM\_032385). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf4. FLJ13352 (Accession NM\_024592) is another VGAM1808 host target gene. FLJ13352 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13352 BINDING SITE, designated SEQ ID:23828, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60264] Another function of VGAM1808 is therefore inhibition of FLJ13352 (Accession NM\_024592). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ13352. FLJ14346 (Accession NM\_025029) is another VGAM1808 host target gene. FLJ14346 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14346 BINDING SITE, designated SEQ ID:24622, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60265] Another function of VGAM1808 is therefore inhibition of FLJ14346 (Accession NM\_025029). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14346. FLJ20073 (Accession NM\_017654) is another VGAM1808 host target gene. FLJ20073 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20073 BINDING SITE, designated SEQ ID:19162, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM



RNA, also designated SEQ ID:4519.

[60266] Another function of VGAM1808 is therefore inhibition of FLJ20073 (Accession NM\_017654). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20073. FLJ22378 (Accession NM\_025078) is another VGAM1808 host target gene. FLJ22378 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22378, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22378 BINDING SITE, designated SEQ ID:24678, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60267] Another function of VGAM1808 is therefore inhibition of FLJ22378 (Accession NM\_025078). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22378. JDD1 (Accession XM\_032515) is another VGAM1808 host target gene. JDD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JDD1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JDD1 BINDING SITE, designated SEQ ID:31670, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60268] Another function of VGAM1808 is therefore inhibition of JDD1 (Accession XM\_032515). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JDD1. Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM\_029962) is another VGAM1808 host target gene. KCNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNT1 BINDING SITE, designated SEQ ID:30972, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60269] Another function of VGAM1808 is therefore inhibition of Potassium Channel, Subfamily T, Member 1 (KCNT1, Ac-

cession XM\_029962). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNT1. KIAA0285 (Accession NM\_014807) is another VGAM1808 host target gene. KIAA0285 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0285 BINDING SITE, designated SEQ ID:16746, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60270] Another function of VGAM1808 is therefore inhibition of KIAA0285 (Accession NM\_014807). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0285. KIAA1764 (Accession XM\_045086) is another VGAM1808 host target gene. KIAA1764 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1764, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1764 BINDING SITE, designated SEQ ID:34353, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60271] Another function of VGAM1808 is therefore inhibition of KIAA1764 (Accession XM\_045086). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1764. MGC2941 (Accession NM\_024297) is another VGAM1808 host target gene. MGC2941 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2941, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2941 BINDING SITE, designated SEQ ID:23577, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60272] Another function of VGAM1808 is therefore inhibition of MGC2941 (Accession NM\_024297). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2941. moblak (Accession NM\_130807) is another

VGAM1808 host target gene. moblak BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by moblak, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of moblak BINDING SITE, designated SEQ ID:28305, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60273] Another function of VGAM1808 is therefore inhibition of moblak (Accession NM\_130807). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with moblak. MSP (Accession NM\_032046) is another VGAM1808 host target gene. MSP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSP BINDING SITE, designated SEQ ID:25760, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60274] Another function of VGAM1808 is therefore inhibition of MSP (Accession NM\_032046). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSP. Myosin, Heavy Polypeptide 10, Non-muscle (MYH10, Accession XM\_044702) is another VGAM1808 host target gene. MYH10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYH10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYH10 BINDING SITE, designated SEQ ID:34260, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60275] Another function of VGAM1808 is therefore inhibition of Myosin, Heavy Polypeptide 10, Non-muscle (MYH10, Accession XM\_044702). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYH10. Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM\_021815) is another VGAM1808 host target gene. SLC5A7 BINDING SITE is HOST TARGET binding site

found in the 3` untranslated region of mRNA encoded by SLC5A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC5A7 BINDING SITE, designated SEQ ID:22387, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60276] Another function of VGAM1808 is therefore inhibition of Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM\_021815). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC5A7. LOC147514 (Accession XM\_041564) is another VGAM1808 host target gene. LOC147514 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC147514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147514 BINDING SITE, designated SEQ ID:33548, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60277] Another function of VGAM1808 is therefore inhibition of LOC147514 (Accession XM\_041564). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147514. LOC157657 (Accession XM\_088352) is another VGAM1808 host target gene. LOC157657 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157657, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157657 BINDING SITE, designated SEQ ID:39629, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60278] Another function of VGAM1808 is therefore inhibition of LOC157657 (Accession XM\_088352). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157657. LOC219347 (Accession XM\_167564) is another VGAM1808 host target gene. LOC219347 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219347, corresponding to a HOST TARGET binding site such as BIND-



ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219347 BINDING SITE, designated SEQ ID:44677, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60279] Another function of VGAM1808 is therefore inhibition of LOC219347 (Accession XM\_167564). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219347. LOC221692 (Accession XM\_166420) is another VGAM1808 host target gene. LOC221692 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221692, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221692 BINDING SITE, designated SEQ ID:44295, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60280] Another function of VGAM1808 is therefore inhibition of LOC221692 (Accession XM\_166420). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221692. LOC63923 (Accession XM\_040527) is another VGAM1808 host target gene. LOC63923 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC63923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC63923 BINDING SITE, designated SEQ ID:33322, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60281] Another function of VGAM1808 is therefore inhibition of LOC63923 (Accession XM\_040527). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC63923. LOC90342 (Accession XM\_031009) is another VGAM1808 host target gene. LOC90342 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90342 BINDING SITE, designated SEQ ID:31255, to the nucleotide sequence of VGAM1808 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4519.

[60282] Another function of VGAM1808 is therefore inhibition of LOC90342 (Accession XM\_031009). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90342. LOC92465 (Accession XM\_045250) is another VGAM1808 host target gene. LOC92465 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92465 BINDING SITE, designated SEQ ID:34392, to the nucleotide sequence of VGAM1808 RNA, herein designated VGAM RNA, also designated SEQ ID:4519.

[60283] Another function of VGAM1808 is therefore inhibition of LOC92465 (Accession XM\_045250). Accordingly, utilities of VGAM1808 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92465. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1809 (VGAM1809) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60284] VGAM1809 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1809 was detected is described hereinabove with reference to Figs. 1–8.

[60285] VGAM1809 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1809 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60286] VGAM1809 gene encodes a VGAM1809 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1809 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1809 precursor RNA is designated SEQ ID:1795, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1795 is located at position 28383 relative to the genome of Rana Tigrina Ranavirus.

[60287] VGAM1809 precursor RNA folds onto itself, forming

VGAM1809 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60288] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1809 folded precursor RNA into VGAM1809 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1809 RNA is designated SEQ ID:4520, and is provided hereinbelow with reference to the sequence listing part.

[60289] VGAM1809 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1809 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1809 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60290] VGAM1809 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1809 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1809 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1809 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1809 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60291] The complementary binding of VGAM1809 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1809 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1809 host target RNA into VGAM1809 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60292] It is appreciated that VGAM1809 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1809 host target genes. The mRNA of each one of this plurality of VGAM1809 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1809 RNA, herein designated VGAM RNA, and which when bound by VGAM1809 RNA causes inhibition of translation of respective one or more VGAM1809 host target proteins.

[60293] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1809 gene, herein designated VGAM GENE, on one or more VGAM1809 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60294] It is yet further appreciated that a function of VGAM1809 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1809 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1809 correlate with, and may be deduced from, the identity of the host target genes which VGAM1809 binds and in-



hibits, and the function of these host target genes, as elaborated hereinbelow.

[60295] Nucleotide sequences of the VGAM1809 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1809 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1809 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1809 are further described hereinbelow with reference to Table 1.

[60296] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1809 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1809 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60297] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1809 gene, herein designated VGAM is inhibition of expression of VGAM1809 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1809 correlate with, and may be deduced from, the identity of the target genes which VGAM1809 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[60298] Telomerase-associated Protein 1 (TEP1, Accession NM\_007110) is a VGAM1809 host target gene. TEP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEP1 BINDING SITE, designated SEQ ID:13975, to the nucleotide sequence of VGAM1809 RNA, herein designated VGAM RNA, also designated SEQ ID:4520.

[60299] A function of VGAM1809 is therefore inhibition of Telomerase-associated Protein 1 (TEP1, Accession NM\_007110), a gene which interacts with active telomerase RNA. Accordingly, utilities of VGAM1809 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEP1. The function of TEP1 has been established by previous studies. The telomerase ribonucleoprotein (OMIM Ref. No. 187270) catalyzes the addition of new telomeres on the chromosome ends. Harrington et al. (1997) noted that in humans, the telomeric repeat is 5-prime-TTAGGG-3-prime and the telomerase RNA contains a sequence complementary to this telomeric repeat.

The telomerase RNA template is required for telomere repeat synthesis in vitro and in vivo. The ribonucleoprotein complex responsible for telomerase activity had been purified only in ciliates. Purified tetrahymena telomerase contains an RNA and 2 protein components, p80 and p95. The p80 component can be specifically cross linked to telomerase RNA, whereas the p95 component binds and cross links to single-stranded, telomeric DNA. Harrington et al. (1997) identified a cDNA encoding a tetrahymena p80 homolog from a murine colonic crypt expressed sequence tag (EST) database. The mouse sequence was used as a probe to identify contiguous human cDNA clones from a library prepared from a human colon carcinoma cell line. The mouse and human open reading frames were found to be 75% identical at the amino acid level. The predicted human polypeptide contains 2,627 amino acids, 2 fewer than the predicted mouse polypeptide. Northern blot analysis of both mouse and human tissues showed widespread expression of the gene, which they symbolized TP1. The studies indicated that telomerase-associated proteins are conserved from ciliates to humans. Saito et al. (1997) mapped the human TEP1 gene and mouse Tep1 gene by fluorescence in situ hybridization to human

chromosome 14q11.2 and to the C2–D1 band of mouse chromosome 14, respectively. By means of genetic linkage mapping, the mouse gene was further localized to a position 2.7 cM distal to D14Mit18 and D14Mit134, and 2.0 cM proximal to D14Mit5 on mouse chromosome 14, where conserved linkage homology with human chromosome 14q11–q12 had been identified.

[60300] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[60301] Harrington, L.; McPhail, T.; Mar, V.; Zhou, W.; Oulton, R.; Bass, M. B.; Arruda, I.; Robinson, M. O. : A mammalian telomerase–associated protein. *Science* 275: 973–976, 1997. ; and

[60302] Saito, T.; Matsuda, Y.; Suzuki, T.; Hayashi, A.; Yuan, X.; Saito, M.; Nakayama, J.; Hori, T.; Ishikawa, F. : Comparative gene mapping of the human and mouse TEP1 genes, which encode one.

[60303] Further studies establishing the function and utilities of TEP1 are found in John Hopkins OMIM database record ID 601686, and in cited publications numbered 6227–6228 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein

265 (ZNF265, Accession NM\_005455) is another VGAM1809 host target gene. ZNF265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF265 BINDING SITE, designated SEQ ID:11937, to the nucleotide sequence of VGAM1809 RNA, herein designated VGAM RNA, also designated SEQ ID:4520.

[60304] Another function of VGAM1809 is therefore inhibition of Zinc Finger Protein 265 (ZNF265, Accession NM\_005455). Accordingly, utilities of VGAM1809 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF265. LOC147837 (Accession XM\_085915) is another VGAM1809 host target gene. LOC147837 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147837, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147837 BINDING SITE, designated SEQ ID:38395, to the nucleotide sequence of

VGAM1809 RNA, herein designated VGAM RNA, also designated SEQ ID:4520.

[60305] Another function of VGAM1809 is therefore inhibition of LOC147837 (Accession XM\_085915). Accordingly, utilities of VGAM1809 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147837. LOC221656 (Accession XM\_166418) is another VGAM1809 host target gene. LOC221656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221656 BINDING SITE, designated SEQ ID:44293, to the nucleotide sequence of VGAM1809 RNA, herein designated VGAM RNA, also designated SEQ ID:4520.

[60306] Another function of VGAM1809 is therefore inhibition of LOC221656 (Accession XM\_166418). Accordingly, utilities of VGAM1809 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221656. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1810 (VGAM1810) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60307] VGAM1810 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1810 was detected is described hereinabove with reference to Figs. 1–8.

[60308] VGAM1810 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1810 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60309] VGAM1810 gene encodes a VGAM1810 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1810 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1810 precursor RNA is designated SEQ ID:1796, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1796 is located at position 128214 relative to the genome of Equine Herpesvirus 1.

[60310] VGAM1810 precursor RNA folds onto itself, forming VGAM1810 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60311] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1810 folded precursor RNA into VGAM1810 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide sequence of VGAM1810 RNA is designated SEQ ID:4521, and is provided hereinbelow with reference to the sequence listing part.

[60312] VGAM1810 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1810 host target RNA, herein designated



VGAM HOST TARGET RNA. VGAM1810 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60313] VGAM1810 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1810 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1810 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1810 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1810 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60314] The complementary binding of VGAM1810 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1810 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1810 host target RNA into VGAM1810 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60315] It is appreciated that VGAM1810 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1810 host target genes. The mRNA of each one of this plurality of VGAM1810 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1810 RNA, herein designated VGAM RNA, and which when bound by VGAM1810 RNA causes inhibition of translation of respective one or more VGAM1810 host target proteins.

[60316] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1810 gene, herein designated VGAM GENE, on one or more VGAM1810 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60317] It is yet further appreciated that a function of VGAM1810 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1810 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1810 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60318] Nucleotide sequences of the VGAM1810 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1810 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1810 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1810 are further described hereinbelow with reference to Table 1.

[60319] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1810 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1810 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60320] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1810 gene, herein designated VGAM is inhibition of expression of VGAM1810 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1810 correlate with, and may be deduced from, the identity of the target genes which VGAM1810

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60321] Inositol Hexaphosphate Kinase 1 (IHPK1, Accession XM\_171045) is a VGAM1810 host target gene. IHPK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IHPK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IHPK1 BINDING SITE, designated SEQ ID:45823, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ ID:4521.

[60322] A function of VGAM1810 is therefore inhibition of Inositol Hexaphosphate Kinase 1 (IHPK1, Accession XM\_171045), a gene which is a messenger molecule that releases calcium from intracellular stores. Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IHPK1. The function of IHPK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1061. Ring Finger Protein 26 (RNF26, Accession NM\_032015) is another VGAM1810 host target gene.

RNF26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF26 BINDING SITE, designated SEQ ID:25728, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ ID:4521.

[60323] Another function of VGAM1810 is therefore inhibition of Ring Finger Protein 26 (RNF26, Accession NM\_032015). Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF26. FLJ10898 (Accession XM\_002486) is another VGAM1810 host target gene. FLJ10898 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10898, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10898 BINDING SITE, designated SEQ ID:29892, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ

ID:4521.

[60324] Another function of VGAM1810 is therefore inhibition of FLJ10898 (Accession XM\_002486). Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10898. KIAA1550 (Accession XM\_039393) is another VGAM1810 host target gene. KIAA1550 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1550, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1550 BINDING SITE, designated SEQ ID:33070, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ ID:4521.

[60325] Another function of VGAM1810 is therefore inhibition of KIAA1550 (Accession XM\_039393). Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1550. Ubiquitin-like, Containing PHD and RING Finger Domains, 1 (UHRF1, Accession NM\_013282) is another VGAM1810 host target gene. UHRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by UHRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UHRF1 BINDING SITE, designated SEQ ID:14951, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ ID:4521.

[60326] Another function of VGAM1810 is therefore inhibition of Ubiquitin-like, Containing PHD and RING Finger Domains, 1 (UHRF1, Accession NM\_013282). Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UHRF1. Ubiquitin Specific Protease 20 (USP20, Accession NM\_006676) is another VGAM1810 host target gene. USP20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP20 BINDING SITE, designated SEQ ID:13502, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ ID:4521.



[60327] Another function of VGAM1810 is therefore inhibition of Ubiquitin Specific Protease 20 (USP20, Accession NM\_006676). Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP20. LOC147299 (Accession XM\_085763) is another VGAM1810 host target gene. LOC147299 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147299 BINDING SITE, designated SEQ ID:38331, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ ID:4521.

[60328] Another function of VGAM1810 is therefore inhibition of LOC147299 (Accession XM\_085763). Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147299. LOC255189 (Accession XM\_172929) is another VGAM1810 host target gene. LOC255189 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255189, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255189 BINDING SITE, designated SEQ ID:46193, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ ID:4521.

[60329] Another function of VGAM1810 is therefore inhibition of LOC255189 (Accession XM\_172929). Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255189. LOC257476 (Accession XM\_028610) is another VGAM1810 host target gene. LOC257476 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257476 BINDING SITE, designated SEQ ID:30715, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ ID:4521.

[60330] Another function of VGAM1810 is therefore inhibition of LOC257476 (Accession XM\_028610). Accordingly, utilities of VGAM1810 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC257476. LOC90917 (Accession XM\_034861) is another VGAM1810 host target gene. LOC90917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90917 BINDING SITE, designated SEQ ID:32167, to the nucleotide sequence of VGAM1810 RNA, herein designated VGAM RNA, also designated SEQ ID:4521.

[60331] Another function of VGAM1810 is therefore inhibition of LOC90917 (Accession XM\_034861). Accordingly, utilities of VGAM1810 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90917. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1811 (VGAM1811) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60332] VGAM1811 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1811 was detected is described hereinabove with reference to Figs. 1–8.

[60333] VGAM1811 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1811 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60334] VGAM1811 gene encodes a VGAM1811 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1811 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1811 precursor RNA is designated SEQ ID:1797, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1797 is located at position 132691 relative to the genome of Equine Herpesvirus 1.

[60335] VGAM1811 precursor RNA folds onto itself, forming VGAM1811 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60336] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1811 folded precursor RNA into VGAM1811 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1811 RNA is designated SEQ ID:4522, and is provided hereinbelow with reference to the sequence listing part.

[60337] VGAM1811 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1811 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1811 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60338] VGAM1811 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1811 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1811 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1811 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1811 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60339] The complementary binding of VGAM1811 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1811 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1811 host target RNA into VGAM1811 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60340] It is appreciated that VGAM1811 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1811 host target genes. The mRNA of each one of this plurality of VGAM1811 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1811 RNA, herein designated VGAM RNA, and which when bound by VGAM1811 RNA causes inhibition of translation of respective one or more VGAM1811 host target proteins.

[60341] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1811 gene, herein designated VGAM GENE, on one or more VGAM1811 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60342] It is yet further appreciated that a function of VGAM1811 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1811 correlate with, and may be deduced from, the identity of the host target genes which VGAM1811 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60343] Nucleotide sequences of the VGAM1811 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the



`diced` VGAM1811 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1811 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1811 are further described hereinbelow with reference to Table 1.

[60344] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1811 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1811 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60345] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1811 gene, herein designated VGAM is inhibition of expression of VGAM1811 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1811 correlate with, and may be deduced from, the identity of the target genes which VGAM1811 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60346] Complement Component 7 (C7, Accession NM\_000587) is a VGAM1811 host target gene. C7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by C7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C7 BINDING SITE, designated SEQ ID:6190, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60347] A function of VGAM1811 is therefore inhibition of Complement Component 7 (C7, Accession NM\_000587). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C7. Cholecystokinin A Receptor (CCKAR, Accession NM\_000730) is another VGAM1811 host target gene. CCKAR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CCKAR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCKAR BINDING SITE, designated SEQ ID:6389, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60348] Another function of VGAM1811 is therefore inhibition of

Cholecystokinin A Receptor (CCKAR, Accession NM\_000730), a gene which Cholecystokinin A receptor, a G protein-coupled receptor; regulates gallbladder contraction and secretion of pancreatic enzymes. Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCKAR. The function of CCKAR has been established by previous studies. The cholecystokinin (CCK) family of peptide hormones (see OMIM Ref. No. 118440) have been implicated in numerous important physiologic events. These appear to be mediated through 2 general classes of receptors, A and B, based on their binding affinities for CCK/gastrin family peptides. Boden et al. (1995) compared the biologic and molecular properties of CCKA and CCKB (OMIM Ref. No. 118445) receptors. Ulrich et al. (1993) noted that, through binding to class A receptors, CCK is a major physiologic mediator of gallbladder contraction and pancreatic enzyme secretion. It appears to play a role in slowing gastric emptying, relaxation of the sphincter of Oddi, and potentiation of insulin secretion. Further, it has been implicated as a mediator of pancreatic growth and tumorigenesis. Class A receptors have also been described in the anterior pituitary, myenteric plexus,

and regions of the central nervous system, where they have been implicated in the pathogenesis of feeding disorders, Parkinson disease, schizophrenia, and drug addiction. Animal model experiments lend further support to the function of CCKAR. ANIMAL MODEL Funakoshi et al. (1995) found a defect in expression of the CCKAR gene in both the fetal and the adult pancreas of a strain of rats (OLETF). They proposed these rats as a useful model for determining CCK receptor function.

[60349] It is appreciated that the abovementioned animal model for CCKAR is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[60350] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[60351] Ulrich, C. D.; Ferber, I.; Holicky, E.; Hadac, E.; Buell, G.; Miller, L. J. : Molecular cloning and functional expression of the human gallbladder cholecystokinin A receptor. Biochem. Biophys. Res. Commun. 193: 204-211, 1993. ; and

[60352] Funakoshi, A.; Miyasaka, K.; Shinozaki, H.; Masuda, M.; Kawanami, T.; Takata, Y.; Kono, A. : An animal model of

congenital defect of gene expression of cholecystokinin (CCK)–A receptor.

[60353] Further studies establishing the function and utilities of CCKAR are found in John Hopkins OMIM database record ID 118444, and in cited publications numbered 336–345 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interferon, Omega 1 (IFNW1, Accession NM\_002177) is another VGAM1811 host target gene. IFNW1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by IFNW1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IFNW1 BINDING SITE, designated SEQ ID:7936, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60354] Another function of VGAM1811 is therefore inhibition of Interferon, Omega 1 (IFNW1, Accession NM\_002177), a gene which may regulate antiviral defence, cell growth, and immune activation. Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IFNW1.

The function of IFNW1 has been established by previous studies. Henco et al. (1985) compiled partial maps of the interferon gene cluster located on 9p21. These maps showed that members of the 2 main families of genes in the IFN superfamily, interferon- $\alpha$  (OMIM Ref. No. 147660) and interferon- $\omega$  (IFNW), are interspersed. Olopade et al. (1992) studied the deletions of the short arm of chromosome 9 frequently observed in acute lymphoblastic leukemia and in gliomas. These deletions often include the entire interferon gene cluster, which comprises about 26 IFNA, IFNW, and IFNB1 (OMIM Ref. No. 147640) genes, as well as the gene for methylthioadenosine phosphorylase (MTAP; 156540). By comparing microscopic deletions with the genes lost at the molecular level, Olopade et al. (1992) determined the order of these genes on 9p to be tel--IFNB1--IFNA/IFNW cluster--MTAP--cen. In a few cell lines and in primary leukemia cells, they observed deletions that had breakpoints within the IFN gene cluster and resulted in partial loss of the IFN genes. These partial deletions allowed them to determine the order of some genes or groups of genes in the IFNA/IFNW gene cluster. From their deletion analysis, Olopade et al. (1992) deduced the following order of the IFN gene on 9p: pter-

--IFNB1--(IFNW1, IFNA21)--IFNWP15--IFNA4--IFNW9--IFNA7--IFNA10--IFNWP18--IFNAP16--IFNA17--IFNA14--(IFNA22, IFNA5, IFNAP20, IFNA6, IFNA13, IFNA2)--(IFNA8, IFNW2, IFNWP19, IFNA1)--MTAP--cen. The genes within the large linkage group are arranged in tandem with their 3-prime end pointing toward the telomere of the short arm. Thus, at least 2 functional interferon-omega genes, IFNW1 and IFNW2, were mapped and several IFNW pseudogenes, e.g., IFNWP15, were localized

[60355] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[60356] Olopade, O. I.; Bohlander, S. K.; Pomykala, H.; Maltepe, E.; Van Melle, E.; Le Beau, M. M.; Diaz, M. O. : Mapping of the shortest region of overlap of deletions of the short arm of chromosome 9 associated with human neoplasia. *Genomics* 14: 437-443, 1992. ; and

[60357] Diaz, M. O.; Bohlander, S. : Nomenclature of the human interferon genes. *J. Interferon Res.* 13: 443-444, 1993.

[60358] Further studies establishing the function and utilities of IFNW1 are found in John Hopkins OMIM database record ID 147553, and in cited publications numbered

4473–4475 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Like-glycosyltransferase (LARGE, Accession NM\_004737) is another VGAM1811 host target gene. LARGE BINDING SITE1 and LARGE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LARGE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LARGE BINDING SITE1 and LARGE BINDING SITE2, designated SEQ ID:11129 and SEQ ID:28601 respectively, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60359] Another function of VGAM1811 is therefore inhibition of Like-glycosyltransferase (LARGE, Accession NM\_004737), a gene which is a member of the N-acetylglucosaminyltransferase family. Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LARGE. The function of LARGE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with



reference to VGAM205. Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM\_022442) is another VGAM1811 host target gene. UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UBE2V1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3, designated SEQ ID:22763, SEQ ID:9364 and SEQ ID:25510 respectively, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60360] Another function of VGAM1811 is therefore inhibition of Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM\_022442), a gene which may play a role in signaling for DNA repair. Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2V1. The function of UBE2V1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM155. DnaJ (Hsp40) Homolog, Subfamily C, Member 5

(DNAJC5, Accession XM\_028966) is another VGAM1811 host target gene. DNAJC5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DNAJC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJC5 BINDING SITE, designated SEQ ID:30810, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60361] Another function of VGAM1811 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily C, Member 5 (DNAJC5, Accession XM\_028966). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJC5. KIAA0367 (Accession XM\_041018) is another VGAM1811 host target gene. KIAA0367 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0367, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0367 BINDING SITE, designated SEQ ID:33420, to the

nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60362] Another function of VGAM1811 is therefore inhibition of KIAA0367 (Accession XM\_041018). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0367. MGC12538 (Accession NM\_032746) is another VGAM1811 host target gene. MGC12538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12538 BINDING SITE, designated SEQ ID:26481, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60363] Another function of VGAM1811 is therefore inhibition of MGC12538 (Accession NM\_032746). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12538. Protocadherin 10 (PCDH10, Accession NM\_032961) is another VGAM1811 host target gene. PCDH10 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by PCDH10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH10 BINDING SITE, designated SEQ ID:26766, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60364] Another function of VGAM1811 is therefore inhibition of Protocadherin 10 (PCDH10, Accession NM\_032961). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH10. Phosphodiesterase 1C, Calmodulin-dependent 70kDa (PDE1C, Accession NM\_005020) is another VGAM1811 host target gene. PDE1C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE1C BINDING SITE, designated SEQ ID:11460, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60365] Another function of VGAM1811 is therefore inhibition of Phosphodiesterase 1C, Calmodulin-dependent 70kDa (PDE1C, Accession NM\_005020). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE1C. STATI2 (Accession XM\_170547) is another VGAM1811 host target gene. STATI2 BINDING SITE1 and STATI2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by STATI2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STATI2 BINDING SITE1 and STATI2 BINDING SITE2, designated SEQ ID:45368 and SEQ ID:9957 respectively, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60366] Another function of VGAM1811 is therefore inhibition of STATI2 (Accession XM\_170547). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STATI2. LOC152059 (Accession XM\_087372) is another VGAM1811 host target gene. LOC152059 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC152059, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152059 BINDING SITE, designated SEQ ID:39207, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60367] Another function of VGAM1811 is therefore inhibition of LOC152059 (Accession XM\_087372). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152059. LOC157507 (Accession XM\_088312) is another VGAM1811 host target gene. LOC157507 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157507, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157507 BINDING SITE, designated SEQ ID:39605, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60368] Another function of VGAM1811 is therefore inhibition of LOC157507 (Accession XM\_088312). Accordingly, utilities

of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157507. LOC157697 (Accession XM\_088365) is another VGAM1811 host target gene. LOC157697 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157697, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157697 BINDING SITE, designated SEQ ID:39645, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60369] Another function of VGAM1811 is therefore inhibition of LOC157697 (Accession XM\_088365). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157697. LOC201252 (Accession XM\_113941) is another VGAM1811 host target gene. LOC201252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC201252 BINDING SITE, designated SEQ ID:42556, to the nucleotide sequence of VGAM1811 RNA, herein designated VGAM RNA, also designated SEQ ID:4522.

[60370] Another function of VGAM1811 is therefore inhibition of LOC201252 (Accession XM\_113941). Accordingly, utilities of VGAM1811 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201252. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1812 (VGAM1812) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60371] VGAM1812 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1812 was detected is described hereinabove with reference to Figs. 1–8.

[60372] VGAM1812 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1812 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.



[60373] VGAM1812 gene encodes a VGAM1812 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1812 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1812 precursor RNA is designated SEQ ID:1798, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1798 is located at position 129486 relative to the genome of Equine Herpesvirus 1.

[60374] VGAM1812 precursor RNA folds onto itself, forming VGAM1812 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60375] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1812 folded precursor RNA into VGAM1812 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1812 RNA is designated SEQ ID:4523, and is provided hereinbelow with reference to the sequence listing part.

[60376] VGAM1812 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1812 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1812 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60377] VGAM1812 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1812 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1812 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1812 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1812 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60378] The complementary binding of VGAM1812 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1812 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1812 host target RNA into VGAM1812 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60379] It is appreciated that VGAM1812 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1812 host target genes. The mRNA of each one of this plurality of VGAM1812 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1812 RNA, herein designated VGAM RNA, and which when bound by VGAM1812 RNA causes inhibition of translation of respective one or more VGAM1812 host target proteins.

[60380] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1812 gene, herein designated VGAM GENE, on one or more VGAM1812 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[60381] It is yet further appreciated that a function of VGAM1812 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1812 correlate with, and may be deduced from, the identity of the host target genes which VGAM1812 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60382] Nucleotide sequences of the VGAM1812 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1812 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1812 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1812 are further described hereinbelow with reference to Table 1.

[60383] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1812 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1812 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60384] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1812 gene, herein designated VGAM is inhibition of expression of VGAM1812 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1812 correlate with, and may be deduced from, the identity of the target genes which VGAM1812 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60385] Breast Cancer 1, Early Onset (BRCA1, Accession NM\_007301) is a VGAM1812 host target gene. BRCA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRCA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRCA1 BINDING SITE, designated SEQ ID:14202, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60386] A function of VGAM1812 is therefore inhibition of Breast

Cancer 1, Early Onset (BRCA1, Accession NM\_007301). Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRCA1. Guanine Nucleotide Binding Protein (G protein), Alpha Activating Activity Polypeptide O (GNAO1, Accession XM\_165653) is another VGAM1812 host target gene. GNAO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAO1 BINDING SITE, designated SEQ ID:43718, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60387] Another function of VGAM1812 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Activating Activity Polypeptide O (GNAO1, Accession XM\_165653), a gene which functions as modulators or transducers in various transmembrane signaling systems. Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAO1. The function of GNAO1 and

its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM665. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 12B (PPP1R12B, Accession NM\_032104) is another VGAM1812 host target gene. PPP1R12B BINDING SITE1 and PPP1R12B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PPP1R12B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R12B BINDING SITE1 and PPP1R12B BINDING SITE2, designated SEQ ID:25796 and SEQ ID:25794 respectively, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60388] Another function of VGAM1812 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 12B (PPP1R12B, Accession NM\_032104). Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R12B. FLJ10922 (Accession NM\_018273) is another VGAM1812 host target gene. FLJ10922 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by FLJ10922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10922 BINDING SITE, designated SEQ ID:20255, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60389] Another function of VGAM1812 is therefore inhibition of FLJ10922 (Accession NM\_018273). Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10922. FLJ12876 (Accession NM\_022754) is another VGAM1812 host target gene. FLJ12876 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12876 BINDING SITE, designated SEQ ID:22986, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60390] Another function of VGAM1812 is therefore inhibition of FLJ12876 (Accession NM\_022754). Accordingly, utilities of

VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12876. KIAA1582 (Accession XM\_037262) is another VGAM1812 host target gene. KIAA1582 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1582, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1582 BINDING SITE, designated SEQ ID:32579, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60391] Another function of VGAM1812 is therefore inhibition of KIAA1582 (Accession XM\_037262). Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1582. Nuclear Factor of Activated T-cells 5, Tonicity-responsive (NFAT5, Accession NM\_138714) is another VGAM1812 host target gene. NFAT5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NFAT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of NFAT5 BINDING SITE, designated SEQ ID:28953, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60392] Another function of VGAM1812 is therefore inhibition of Nuclear Factor of Activated T-cells 5, Tonicity-responsive (NFAT5, Accession NM\_138714). Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFAT5. LOC151568 (Accession NM\_138483) is another VGAM1812 host target gene. LOC151568 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151568 BINDING SITE, designated SEQ ID:28837, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60393] Another function of VGAM1812 is therefore inhibition of LOC151568 (Accession NM\_138483). Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC151568. LOC199986 (Accession XM\_117168) is another VGAM1812 host target gene. LOC199986 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199986, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199986 BINDING SITE, designated SEQ ID:43271, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60394] Another function of VGAM1812 is therefore inhibition of LOC199986 (Accession XM\_117168). Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199986. LOC255057 (Accession XM\_170903) is another VGAM1812 host target gene. LOC255057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255057 BINDING SITE, designated SEQ ID:45660, to the nucleotide sequence of VGAM1812 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4523.

[60395] Another function of VGAM1812 is therefore inhibition of LOC255057 (Accession XM\_170903). Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255057. LOC91801 (Accession NM\_138775) is another VGAM1812 host target gene. LOC91801 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91801, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91801 BINDING SITE, designated SEQ ID:29009, to the nucleotide sequence of VGAM1812 RNA, herein designated VGAM RNA, also designated SEQ ID:4523.

[60396] Another function of VGAM1812 is therefore inhibition of LOC91801 (Accession NM\_138775). Accordingly, utilities of VGAM1812 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91801. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1813 (VGAM1813) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60397] VGAM1813 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1813 was detected is described hereinabove with reference to Figs. 1–8.

[60398] VGAM1813 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1813 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60399] VGAM1813 gene encodes a VGAM1813 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1813 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1813 precursor RNA is designated SEQ ID:1799, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1799 is located at position 137114 relative to the genome of Equine Herpesvirus 1.

[60400] VGAM1813 precursor RNA folds onto itself, forming

VGAM1813 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60401] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1813 folded precursor RNA into VGAM1813 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM1813 RNA is designated SEQ ID:4524, and is provided hereinbelow with reference to the sequence listing part.

[60402] VGAM1813 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1813 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1813 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[60403] VGAM1813 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1813 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1813 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1813 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1813 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example



only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60404] The complementary binding of VGAM1813 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1813 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1813 host target RNA into VGAM1813 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60405] It is appreciated that VGAM1813 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1813 host target genes. The mRNA of each one of this plurality of VGAM1813 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1813 RNA, herein designated VGAM RNA, and which when bound by VGAM1813 RNA causes inhibition of translation of respective one or more VGAM1813 host target proteins.

[60406] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1813 gene, herein designated VGAM GENE, on one or more VGAM1813 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60407] It is yet further appreciated that a function of VGAM1813 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1813 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1813 correlate with, and may be deduced from, the identity of the host target genes which VGAM1813 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[60408] Nucleotide sequences of the VGAM1813 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1813 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1813 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1813 are further described hereinbelow with reference to Table 1.

[60409] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1813 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1813 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60410] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1813 gene, herein designated VGAM is inhibition of expression of VGAM1813 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1813 correlate with, and may be deduced from, the identity of the target genes which VGAM1813 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[60411] Mitogen-activated Protein Kinase 14 (MAPK14, Accession NM\_001315) is a VGAM1813 host target gene. MAPK14 BINDING SITE1 through MAPK14 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPK14, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK14 BINDING SITE1 through MAPK14 BINDING SITE4, designated SEQ ID:7003, SEQ ID:29107, SEQ ID:29110 and SEQ ID:29114 respectively, to the nucleotide sequence of VGAM1813 RNA, herein designated VGAM RNA, also designated SEQ ID:4524.

[60412] A function of VGAM1813 is therefore inhibition of Mitogen-activated Protein Kinase 14 (MAPK14, Accession NM\_001315), a gene which is important for cytokine production; responds to changes in extracellular osmolarity. Accordingly, utilities of VGAM1813 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK14. The function of MAPK14 and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM107.KIAA1110 (Accession XM\_029973) is another VGAM1813 host target gene. KIAA1110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1110 BINDING SITE, designated SEQ ID:30982, to the nucleotide sequence of VGAM1813 RNA, herein designated VGAM RNA, also designated SEQ ID:4524.

[60413] Another function of VGAM1813 is therefore inhibition of KIAA1110 (Accession XM\_029973). Accordingly, utilities of VGAM1813 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1110. LOC146315 (Accession XM\_027576) is another VGAM1813 host target gene. LOC146315 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146315, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146315 BINDING SITE, designated SEQ ID:30533, to

the nucleotide sequence of VGAM1813 RNA, herein designated VGAM RNA, also designated SEQ ID:4524.

[60414] Another function of VGAM1813 is therefore inhibition of LOC146315 (Accession XM\_027576). Accordingly, utilities of VGAM1813 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146315. LOC256158 (Accession XM\_175125) is another VGAM1813 host target gene. LOC256158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE, designated SEQ ID:46621, to the nucleotide sequence of VGAM1813 RNA, herein designated VGAM RNA, also designated SEQ ID:4524.

[60415] Another function of VGAM1813 is therefore inhibition of LOC256158 (Accession XM\_175125). Accordingly, utilities of VGAM1813 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256158. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1814 (VGAM1814) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60416] VGAM1814 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1814 was detected is described hereinabove with reference to Figs. 1–8.

[60417] VGAM1814 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1814 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60418] VGAM1814 gene encodes a VGAM1814 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1814 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1814 precursor RNA is designated SEQ ID:1800, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1800 is located at position 127841 relative to the genome of Equine Herpesvirus 1.

[60419] VGAM1814 precursor RNA folds onto itself, forming VGAM1814 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60420] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1814 folded precursor RNA into VGAM1814 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 90%) nucleotide sequence of VGAM1814 RNA is designated SEQ ID:4525, and is provided hereinbelow with reference to the sequence listing part.

[60421] VGAM1814 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1814 host target RNA, herein designated



VGAM HOST TARGET RNA. VGAM1814 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[60422] VGAM1814 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1814 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1814 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1814 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1814 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60423] The complementary binding of VGAM1814 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1814 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1814 host target RNA into VGAM1814 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60424] It is appreciated that VGAM1814 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1814 host target genes. The mRNA of each one of this plurality of VGAM1814 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1814 RNA, herein designated VGAM RNA, and which when bound by VGAM1814 RNA causes inhibition of translation of respective one or more VGAM1814 host target proteins.

[60425] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1814 gene, herein designated VGAM GENE, on one or more VGAM1814 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60426] It is yet further appreciated that a function of VGAM1814 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1814 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1814 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1814 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60427] Nucleotide sequences of the VGAM1814 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1814 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1814 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1814 are further described hereinbelow with reference to Table 1.

[60428] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1814 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1814 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60429] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1814 gene, herein designated VGAM is inhibition of expression of VGAM1814 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1814 correlate with, and may be deduced from, the identity of the target genes which VGAM1814

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60430] KH Domain Containing, RNA Binding, Signal Transduction Associated 1 (KHDRBS1, Accession NM\_006559) is a VGAM1814 host target gene. KHDRBS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KHDRBS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KHDRBS1 BINDING SITE, designated SEQ ID:13327, to the nucleotide sequence of VGAM1814 RNA, herein designated VGAM RNA, also designated SEQ ID:4525.

[60431] A function of VGAM1814 is therefore inhibition of KH Domain Containing, RNA Binding, Signal Transduction Associated 1 (KHDRBS1, Accession NM\_006559). Accordingly, utilities of VGAM1814 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KHDRBS1. MGC3222 (Accession NM\_024334) is another VGAM1814 host target gene. MGC3222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3222, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3222 BINDING SITE, designated SEQ ID:23641, to the nucleotide sequence of VGAM1814 RNA, herein designated VGAM RNA, also designated SEQ ID:4525.

[60432] Another function of VGAM1814 is therefore inhibition of MGC3222 (Accession NM\_024334). Accordingly, utilities of VGAM1814 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3222. PRO2198 (Accession NM\_018621) is another VGAM1814 host target gene. PRO2198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2198 BINDING SITE, designated SEQ ID:20694, to the nucleotide sequence of VGAM1814 RNA, herein designated VGAM RNA, also designated SEQ ID:4525.

[60433] Another function of VGAM1814 is therefore inhibition of PRO2198 (Accession NM\_018621). Accordingly, utilities of VGAM1814 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PRO2198. LOC200339 (Accession XM\_117226) is another VGAM1814 host target gene. LOC200339 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200339, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200339 BINDING SITE, designated SEQ ID:43299, to the nucleotide sequence of VGAM1814 RNA, herein designated VGAM RNA, also designated SEQ ID:4525.

[60434] Another function of VGAM1814 is therefore inhibition of LOC200339 (Accession XM\_117226). Accordingly, utilities of VGAM1814 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200339. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1815 (VGAM1815) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60435] VGAM1815 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1815 was detected is described hereinabove with reference to Figs. 1–8.

[60436] VGAM1815 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1815 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60437] VGAM1815 gene encodes a VGAM1815 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1815 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1815 precursor RNA is designated SEQ ID:1801, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1801 is located at position 130995 relative to the genome of Equine Herpesvirus 1.

[60438] VGAM1815 precursor RNA folds onto itself, forming VGAM1815 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide



sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60439] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1815 folded precursor RNA into VGAM1815 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1815 RNA is designated SEQ ID:4526, and is provided hereinbelow with reference to the sequence listing part.

[60440] VGAM1815 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1815 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1815 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60441] VGAM1815 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1815 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1815 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1815 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1815 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[60442] The complementary binding of VGAM1815 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1815 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1815 host target RNA into VGAM1815 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60443] It is appreciated that VGAM1815 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1815 host target genes. The mRNA of each one of this plurality of VGAM1815 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1815 RNA, herein designated VGAM RNA, and which when bound by VGAM1815 RNA causes inhibition of translation of respective one or more VGAM1815 host target proteins.

[60444] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1815 gene, herein designated VGAM GENE, on one or more VGAM1815 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60445] It is yet further appreciated that a function of VGAM1815 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1815 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1815 correlate with, and may be deduced from, the identity of the host target genes which VGAM1815 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60446] Nucleotide sequences of the VGAM1815 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1815 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1815 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1815 are further described hereinbelow with reference to Table 1.

[60447] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1815 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1815 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60448] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1815 gene, herein designated VGAM is inhibition of expression of VGAM1815 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1815 correlate with, and may be deduced from, the identity of the target genes which VGAM1815 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60449] Engrailed Homolog 1 (EN1, Accession NM\_001426) is a VGAM1815 host target gene. EN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EN1, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EN1 BINDING SITE, designated SEQ ID:7139, to the nucleotide sequence of VGAM1815 RNA, herein designated VGAM RNA, also designated SEQ ID:4526.

[60450] A function of VGAM1815 is therefore inhibition of Engrailed Homolog 1 (EN1, Accession NM\_001426), a gene which is a member of the homeodomain family of DNA binding proteins; may regulate gene expression, morphogenesis, and differentiation;. Accordingly, utilities of VGAM1815 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EN1. The function of EN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1615. Mannosidase, Alpha, Class 2A, Member 1 (MAN2A1, Accession NM\_002372) is another VGAM1815 host target gene. MAN2A1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MAN2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of MAN2A1 BINDING SITE, designated SEQ ID:8178, to the nucleotide sequence of VGAM1815 RNA, herein designated VGAM RNA, also designated SEQ ID:4526.

[60451] Another function of VGAM1815 is therefore inhibition of Mannosidase, Alpha, Class 2A, Member 1 (MAN2A1, Accession NM\_002372), a gene which catalyzes the final hydrolytic step in the asparagine-linked oligosaccharide (N-glycan) maturation pathway. Accordingly, utilities of VGAM1815 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN2A1. The function of MAN2A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1410. Netrin 4 (NTN4, Accession XM\_031896) is another VGAM1815 host target gene. NTN4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NTN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTN4 BINDING SITE, designated SEQ ID:31511, to the nucleotide sequence of VGAM1815 RNA, herein

designated VGAM RNA, also designated SEQ ID:4526.

[60452] Another function of VGAM1815 is therefore inhibition of Netrin 4 (NTN4, Accession XM\_031896). Accordingly, utilities of VGAM1815 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTN4. Rabip4R (Accession NM\_017987) is another VGAM1815 host target gene. Rabip4R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Rabip4R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rabip4R BINDING SITE, designated SEQ ID:19716, to the nucleotide sequence of VGAM1815 RNA, herein designated VGAM RNA, also designated SEQ ID:4526.

[60453] Another function of VGAM1815 is therefore inhibition of Rabip4R (Accession NM\_017987). Accordingly, utilities of VGAM1815 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rabip4R. LOC143384 (Accession XM\_084504) is another VGAM1815 host target gene. LOC143384 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143384, corresponding



to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143384 BINDING SITE, designated SEQ ID:37614, to the nucleotide sequence of VGAM1815 RNA, herein designated VGAM RNA, also designated SEQ ID:4526.

[60454] Another function of VGAM1815 is therefore inhibition of LOC143384 (Accession XM\_084504). Accordingly, utilities of VGAM1815 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143384. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1816 (VGAM1816) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60455] VGAM1816 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1816 was detected is described hereinabove with reference to Figs. 1-8.

[60456] VGAM1816 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus.

VGAM1816 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60457] VGAM1816 gene encodes a VGAM1816 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1816 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1816 precursor RNA is designated SEQ ID:1802, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1802 is located at position 41903 relative to the genome of Camelpox Virus.

[60458] VGAM1816 precursor RNA folds onto itself, forming VGAM1816 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60459] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1816 folded precursor RNA into VGAM1816 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1816 RNA is designated SEQ ID:4527, and is provided hereinbelow with reference to the sequence listing part.

[60460] VGAM1816 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1816 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1816 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60461] VGAM1816 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1816 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1816 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1816 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1816 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60462] The complementary binding of VGAM1816 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1816 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1816 host target RNA into VGAM1816 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60463] It is appreciated that VGAM1816 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1816 host target genes. The mRNA of each one of this plurality of VGAM1816 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1816 RNA, herein designated VGAM RNA, and which when bound by VGAM1816 RNA causes inhibition of translation of respective one or more VGAM1816 host target proteins.

[60464] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1816 gene, herein designated VGAM GENE, on one or more VGAM1816 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60465] It is yet further appreciated that a function of VGAM1816 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1816 correlate with, and may be deduced from, the identity of the host target genes which VGAM1816 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60466] Nucleotide sequences of the VGAM1816 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1816 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1816 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1816 are further described hereinbelow with reference to Table 1.

[60467] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1816 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1816 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60468] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1816 gene, herein designated VGAM is inhibition of expression of VGAM1816 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1816 correlate with, and may be deduced from, the identity of the target genes which VGAM1816 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60469] Four and A Half LIM Domains 1 (FHL1, Accession NM\_001449) is a VGAM1816 host target gene. FHL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHL1 BINDING SITE, designated SEQ ID:7181, to the nu-

cleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60470] A function of VGAM1816 is therefore inhibition of Four and A Half LIM Domains 1 (FHL1, Accession NM\_001449), a gene which may have an involvement in muscle development or hypertrophy. Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHL1. The function of FHL1 has been established by previous studies. LIM proteins, named for 'LIN11, ISL1, and MEC3,' are defined by the possession of a highly conserved double zinc finger motif, called the LIM domain. Morgan et al. (1995) identified a partial human SLIM1 cDNA. They found that SLIM1 is a developmentally regulated protein that is expressed in human skeletal muscle but not in a variety of other tissues. By searching sequence databases with the partial SLIM1 cDNA isolated by Morgan et al. (1995), Morgan and Madgwick (1996) identified human cDNAs encoding the complete SLIM1 amino acid sequence. The predicted 280-amino acid protein contains 4 LIM domains and a novel single zinc finger domain in the N-terminal region. By Northern blot analysis, SLIM1 is expressed as a 2.3-kb mRNA in human masseter muscle. By somatic cell



hybrid mapping, fluorescence in situ hybridization, and radiation hybrid mapping, Lee et al. (1998) assigned the FHL1 gene to Xq27.2.

[60471] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[60472] Lee, S. M. Y.; Tsui, S. K. W.; Chan, K. K.; Garcia-Barcelo, M.; Waye, M. M. Y.; Fung, K. P.; Liew, C. C.; Lee, C. Y. : Chromosomal mapping, tissue distribution and cDNA sequence of four-and-a-half LIM domain protein 1 (FHL1). Gene 216: 163–170, 1998. ; and

[60473] Morgan, M. J.; Madgwick, A. J.; Charleston, B.; Pell, J. M.; Loughna, P. T. : The developmental regulation of a novel muscle LIM–protein. Biochem. Biophys. Res. Commun. 212: 840–846, 19.

[60474] Further studies establishing the function and utilities of FHL1 are found in John Hopkins OMIM database record ID 300163, and in cited publications numbered 11003–11005 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM\_000838) is another VGAM1816 host target gene. GRM1 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by GRM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM1 BINDING SITE, designated SEQ ID:6498, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60475] Another function of VGAM1816 is therefore inhibition of Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM\_000838), a gene which promotes phosphoinositide hydrolysis. Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM1. The function of GRM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM786. Plakophilin 2 (PKP2, Accession NM\_004572) is another VGAM1816 host target gene. PKP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKP2 BINDING

SITE, designated SEQ ID:10915, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60476] Another function of VGAM1816 is therefore inhibition of Plakophilin 2 (PKP2, Accession NM\_004572), a gene which may play a role in junctional plaques. Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKP2. The function of PKP2 has been established by previous studies. Plakophilins are armadillo repeat-containing proteins that are localized in the desmosomal plaque and cell nucleus. Desmosomal plakophilins, like plakophilin 2, form part of the link between the cytoplasmic tail of cadherins and the intermediate filament cytoskeleton (Bonne et al., 2000). Mertens et al. (1996) isolated cDNAs encoding 2 forms of plakophilin-2 (PKP2), which they named PKP2a and PKP2b, from human colon carcinoma and heart cDNA libraries. The predicted 837-amino acid PKP2a protein contains 9 complete copies of the armadillo motif, which is an approximately 42-amino acid domain first defined in the *Drosophila* 'armadillo' gene product. Compared with PKP2a, the predicted 881-amino acid PKP2b protein contains an insertion of 44 amino acids between

the second and third armadillo motifs. The authors suggested that PKP2a and PKP2b are derived from alternatively spliced PKP2 transcripts. The PKP2 and PKP1 (OMIM Ref. No. 601975) proteins are 42% identical in the armadillo repeats. Immunoblot analysis of a wide range of human cell lines and tissues using antibodies against PKP2 detected an approximately 100-kD protein, which sometimes appeared as a twin band. Immunolocalization studies showed that PKP2 is a constituent of the desmosomal plaque in simple epithelia, some stratified epithelia, and some nonepithelial cells. PKP2 is also enriched in the karyoplasm of cells of various types, including those lacking desmosomes. Northern blot analysis detected approximately 5.3-kb PKP2 transcripts in diverse human cell lines and tissues representing both epithelial and nonepithelial cells. By fluorescence in situ hybridization and analysis of a somatic cell hybrid mapping panel, Bonne et al. (1998) mapped the PKP2 gene to 12p13. Schmidt et al. (1999) used FISH to map the PKP2 gene to 12p11. Further analysis by Bonne et al. (2000) of a human 12p13-specific PAC clone showed that 12p13 was the location of a processed plakophilin-2 pseudogene, PKP2P1. By fluorescence in situ hybridization, Bonne et al. (2000) confirmed

the localization of PKP2 to 12p11.

[60477] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[60478] Bonne, S.; van Hengel, J; van Roy, F. : Assignment of the plakophilin-2 gene (PKP2) and a plakophilin-2 pseudo-gene (PKP2P1) to human chromosome bands 12p11 and 12p13, respectively, by in situ hybridization. Cytogenet. Cell Genet. 88: 286-287, 2000. ; and

[60479] Bonne, S.; van Hengel, J.; van Roy, F. : Chromosomal mapping of human armadillo genes belonging to the p120(ctn)/plakophilin subfamily. Genomics 51: 452-454, 1998.

[60480] Further studies establishing the function and utilities of PKP2 are found in John Hopkins OMIM database record ID 602861, and in cited publications numbered 532 and 7029-5322 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Reticulocalbin 1, EF-hand Calcium Binding Domain (RCN1, Accession XM\_006320) is another VGAM1816 host target gene. RCN1 BINDING SITE1 and RCN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RCN1, corresponding

to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RCN1 BINDING SITE1 and RCN1 BINDING SITE2, designated SEQ ID:29996 and SEQ ID:8804 respectively, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60481] Another function of VGAM1816 is therefore inhibition of Reticulocalbin 1, EF-hand Calcium Binding Domain (RCN1, Accession XM\_006320), a gene which may regulate calcium-dependent activities in the ER lumen or post-ER compartment. Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RCN1. The function of RCN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM865. TEM6 (Accession NM\_022748) is another VGAM1816 host target gene. TEM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of TEM6 BINDING SITE, designated SEQ ID:22967, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60482] Another function of VGAM1816 is therefore inhibition of TEM6 (Accession NM\_022748), a gene which displays elevated expression during tumor angiogenesis. Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM6. The function of TEM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM175.BTB (POZ) Domain Containing 3 (BTBD3, Accession NM\_014962) is another VGAM1816 host target gene. BTBD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTBD3 BINDING SITE, designated SEQ ID:17340, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60483] Another function of VGAM1816 is therefore inhibition of

BTB (POZ) Domain Containing 3 (BTBD3, Accession NM\_014962). Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTBD3. Signal Sequence Receptor, Gamma (translocon-associated protein gamma) (SSR3, Accession NM\_007107) is another VGAM1816 host target gene. SSR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSR3 BINDING SITE, designated SEQ ID:13969, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60484] Another function of VGAM1816 is therefore inhibition of Signal Sequence Receptor, Gamma (translocon-associated protein gamma) (SSR3, Accession NM\_007107). Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSR3. SUN1 (Accession NM\_025154) is another VGAM1816 host target gene. SUN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region



of mRNA encoded by SUN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUN1 BINDING SITE, designated SEQ ID:24794, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60485] Another function of VGAM1816 is therefore inhibition of SUN1 (Accession NM\_025154). Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUN1. LOC125228 (Accession XM\_058913) is another VGAM1816 host target gene. LOC125228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC125228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC125228 BINDING SITE, designated SEQ ID:36794, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60486] Another function of VGAM1816 is therefore inhibition of LOC125228 (Accession XM\_058913). Accordingly, utilities

of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC125228. LOC158563 (Accession XM\_088606) is another VGAM1816 host target gene. LOC158563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158563 BINDING SITE, designated SEQ ID:39871, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60487] Another function of VGAM1816 is therefore inhibition of LOC158563 (Accession XM\_088606). Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158563. LOC161635 (Accession XM\_172921) is another VGAM1816 host target gene. LOC161635 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC161635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC161635 BINDING SITE, designated SEQ ID:46188, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60488] Another function of VGAM1816 is therefore inhibition of LOC161635 (Accession XM\_172921). Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161635. LOC257206 (Accession XM\_173136) is another VGAM1816 host target gene. LOC257206 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257206, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257206 BINDING SITE, designated SEQ ID:46386, to the nucleotide sequence of VGAM1816 RNA, herein designated VGAM RNA, also designated SEQ ID:4527.

[60489] Another function of VGAM1816 is therefore inhibition of LOC257206 (Accession XM\_173136). Accordingly, utilities of VGAM1816 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257206. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1817 (VGAM1817) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60490] VGAM1817 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1817 was detected is described hereinabove with reference to Figs. 1–8.

[60491] VGAM1817 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1817 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60492] VGAM1817 gene encodes a VGAM1817 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1817 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1817 precursor RNA is designated SEQ ID:1803, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1803 is located at position 27215 relative to the

genome of Variola Virus.

[60493] VGAM1817 precursor RNA folds onto itself, forming VGAM1817 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60494] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1817 folded precursor RNA into VGAM1817 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 78%) nucleotide sequence of VGAM1817 RNA is designated SEQ ID:4528, and is provided hereinbelow with reference to the sequence listing part.

[60495] VGAM1817 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1817 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1817 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[60496] VGAM1817 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1817 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1817 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1817 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1817 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60497] The complementary binding of VGAM1817 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1817 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1817 host target RNA into VGAM1817 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60498] It is appreciated that VGAM1817 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1817 host target genes. The mRNA of each one of this plurality of VGAM1817 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1817 RNA, herein designated VGAM RNA, and which when bound by VGAM1817 RNA causes inhibition of translation of respective one or more VGAM1817 host target proteins.

[60499] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1817 gene, herein designated VGAM GENE, on one or more VGAM1817 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60500] It is yet further appreciated that a function of VGAM1817 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1817 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1817 correlate



with, and may be deduced from, the identity of the host target genes which VGAM1817 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60501] Nucleotide sequences of the VGAM1817 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1817 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1817 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1817 are further described hereinbelow with reference to Table 1.

[60502] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1817 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1817 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60503] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1817 gene, herein designated VGAM is inhibition of expression of VGAM1817 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1817 correlate with, and may be deduced

from, the identity of the target genes which VGAM1817 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60504] Collagen, Type IV, Alpha 4 (COL4A4, Accession NM\_000092) is a VGAM1817 host target gene. COL4A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL4A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A4 BINDING SITE, designated SEQ ID:5554, to the nucleotide sequence of VGAM1817 RNA, herein designated VGAM RNA, also designated SEQ ID:4528.

[60505] A function of VGAM1817 is therefore inhibition of Collagen, Type IV, Alpha 4 (COL4A4, Accession NM\_000092). Accordingly, utilities of VGAM1817 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A4. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM\_033332) is another VGAM1817 host target gene. CDC14B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

CDC14B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE, designated SEQ ID:27172, to the nucleotide sequence of VGAM1817 RNA, herein designated VGAM RNA, also designated SEQ ID:4528.

[60506] Another function of VGAM1817 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM\_033332). Accordingly, utilities of VGAM1817 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. FLJ23120 (Accession XM\_097961) is another VGAM1817 host target gene. FLJ23120 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23120 BINDING SITE, designated SEQ ID:41267, to the nucleotide sequence of VGAM1817 RNA, herein designated VGAM RNA, also designated SEQ ID:4528.

[60507] Another function of VGAM1817 is therefore inhibition of

FLJ23120 (Accession XM\_097961). Accordingly, utilities of VGAM1817 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23120. KIAA0738 (Accession NM\_014719) is another VGAM1817 host target gene. KIAA0738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0738 BINDING SITE, designated SEQ ID:16277, to the nucleotide sequence of VGAM1817 RNA, herein designated VGAM RNA, also designated SEQ ID:4528.

[60508] Another function of VGAM1817 is therefore inhibition of KIAA0738 (Accession NM\_014719). Accordingly, utilities of VGAM1817 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0738. KIAA1239 (Accession XM\_049078) is another VGAM1817 host target gene. KIAA1239 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1239, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1239 BINDING SITE, designated SEQ ID:35341, to the nucleotide sequence of VGAM1817 RNA, herein designated VGAM RNA, also designated SEQ ID:4528.

[60509] Another function of VGAM1817 is therefore inhibition of KIAA1239 (Accession XM\_049078). Accordingly, utilities of VGAM1817 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1239. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1818 (VGAM1818) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60510] VGAM1818 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1818 was detected is described hereinabove with reference to Figs. 1–8.

[60511] VGAM1818 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus.

VGAM1818 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[60512] VGAM1818 gene encodes a VGAM1818 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1818 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1818 precursor RNA is designated SEQ ID:1804, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1804 is located at position 28707 relative to the genome of Variola Virus.

[60513] VGAM1818 precursor RNA folds onto itself, forming VGAM1818 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60514] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1818 folded precursor RNA into VGAM1818 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1818 RNA is designated SEQ ID:4529, and is provided hereinbelow with reference to the sequence listing part.

[60515] VGAM1818 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1818 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1818 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60516] VGAM1818 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1818 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1818 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1818 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1818 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60517] The complementary binding of VGAM1818 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1818 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1818 host target RNA into VGAM1818 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[60518] It is appreciated that VGAM1818 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1818 host target genes. The mRNA of each one of this plurality of VGAM1818 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1818 RNA, herein designated VGAM RNA, and which when bound by VGAM1818 RNA causes inhibition of translation of respective one or more VGAM1818 host target proteins.

[60519] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1818 gene, herein designated VGAM GENE, on one or more VGAM1818 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60520] It is yet further appreciated that a function of VGAM1818 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1818 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1818 correlate with, and may be deduced from, the identity of the host target genes which VGAM1818 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60521] Nucleotide sequences of the VGAM1818 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1818 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1818 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1818 are further described hereinbelow with reference to Table 1.

[60522] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1818 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1818 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60523] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1818 gene, herein designated VGAM is inhibition of expression of VGAM1818 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1818 correlate with, and may be deduced from, the identity of the target genes which VGAM1818 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60524] OSRF (Accession XM\_003724) is a VGAM1818 host target gene. OSRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSRF BINDING SITE, designated SEQ ID:29941, to the nucleotide sequence of VGAM1818 RNA, herein designated VGAM RNA, also designated SEQ ID:4529.

[60525] A function of VGAM1818 is therefore inhibition of OSRF

(Accession XM\_003724). Accordingly, utilities of VGAM1818 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSRF. POPX1 (Accession NM\_014906) is another VGAM1818 host target gene. POPX1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by POPX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POPX1 BINDING SITE, designated SEQ ID:17116, to the nucleotide sequence of VGAM1818 RNA, herein designated VGAM RNA, also designated SEQ ID:4529.

[60526] Another function of VGAM1818 is therefore inhibition of POPX1 (Accession NM\_014906). Accordingly, utilities of VGAM1818 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POPX1. LOC124045 (Accession XM\_071873) is another VGAM1818 host target gene. LOC124045 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC124045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC124045 BINDING SITE, designated SEQ ID:37439, to the nucleotide sequence of VGAM1818 RNA, herein designated VGAM RNA, also designated SEQ ID:4529.

[60527] Another function of VGAM1818 is therefore inhibition of LOC124045 (Accession XM\_071873). Accordingly, utilities of VGAM1818 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124045. LOC150848 (Accession XM\_097959) is another VGAM1818 host target gene. LOC150848 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150848 BINDING SITE, designated SEQ ID:41253, to the nucleotide sequence of VGAM1818 RNA, herein designated VGAM RNA, also designated SEQ ID:4529.

[60528] Another function of VGAM1818 is therefore inhibition of LOC150848 (Accession XM\_097959). Accordingly, utilities of VGAM1818 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150848. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1819 (VGAM1819) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60529] VGAM1819 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1819 was detected is described hereinabove with reference to Figs. 1–8.

[60530] VGAM1819 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus. VGAM1819 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60531] VGAM1819 gene encodes a VGAM1819 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1819 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1819 precursor RNA is designated SEQ ID:1805, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1805 is located at position 7183 relative to the genome of Cryphonectria Hypovirus.

[60532] VGAM1819 precursor RNA folds onto itself, forming VGAM1819 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60533] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1819 folded precursor RNA into VGAM1819 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1819 RNA is designated SEQ ID:4530, and is provided hereinbelow with reference to the sequence listing part.

[60534] VGAM1819 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1819 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1819 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60535] VGAM1819 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1819 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1819 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1819 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1819 host target RNA,



herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[60536] The complementary binding of VGAM1819 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1819 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1819 host target RNA into VGAM1819 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60537] It is appreciated that VGAM1819 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1819 host target genes. The mRNA of each one of this plurality of VGAM1819 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1819 RNA, herein designated VGAM RNA, and which when bound by VGAM1819 RNA causes inhibition of translation of respective one or more

VGAM1819 host target proteins.

[60538] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1819 gene, herein designated VGAM GENE, on one or more VGAM1819 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60539] It is yet further appreciated that a function of VGAM1819 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1819 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus.

Specific functions, and accordingly utilities, of VGAM1819 correlate with, and may be deduced from, the identity of the host target genes which VGAM1819 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60540] Nucleotide sequences of the VGAM1819 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1819 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1819 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1819 are further described hereinbelow with reference to Table 1.

[60541] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1819 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1819 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60542] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1819 gene, herein designated VGAM is inhibition of expression of VGAM1819 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1819 correlate with, and may be deduced from, the identity of the target genes which VGAM1819 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60543] Transmembrane Protease, Serine 3 (TMPRSS3, Accession NM\_024022) is a VGAM1819 host target gene. TMPRSS3 BINDING SITE1 through TMPRSS3 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TMPRSS3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMPRSS3 BINDING SITE1 through TMPRSS3 BINDING SITE3, designated SEQ ID:23451, SEQ ID:26187 and SEQ ID:26189 respectively, to the nucleotide sequence of VGAM1819 RNA, herein designated VGAM RNA, also designated SEQ ID:4530.

[60544] A function of VGAM1819 is therefore inhibition of Transmembrane Protease, Serine 3 (TMPRSS3, Accession NM\_024022). Accordingly, utilities of VGAM1819 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMPRSS3. KIAA0757 (Accession NM\_006038) is another VGAM1819 host target gene. KIAA0757 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by KIAA0757, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0757 BINDING SITE, designated SEQ ID:12673, to the nucleotide sequence of VGAM1819 RNA, herein designated VGAM RNA, also designated SEQ ID:4530.

[60545] Another function of VGAM1819 is therefore inhibition of KIAA0757 (Accession NM\_006038). Accordingly, utilities of VGAM1819 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0757. KIAA0828 (Accession XM\_088105) is another VGAM1819 host target gene. KIAA0828 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0828 BINDING SITE, designated SEQ ID:39512, to the nucleotide sequence of VGAM1819 RNA, herein designated VGAM RNA, also designated SEQ ID:4530.

[60546] Another function of VGAM1819 is therefore inhibition of

KIAA0828 (Accession XM\_088105). Accordingly, utilities of VGAM1819 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0828. LOC51133 (Accession NM\_016121) is another VGAM1819 host target gene. LOC51133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51133 BINDING SITE, designated SEQ ID:18206, to the nucleotide sequence of VGAM1819 RNA, herein designated VGAM RNA, also designated SEQ ID:4530.

[60547] Another function of VGAM1819 is therefore inhibition of LOC51133 (Accession NM\_016121). Accordingly, utilities of VGAM1819 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51133. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1820 (VGAM1820) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[60548] VGAM1820 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1820 was detected is described hereinabove with reference to Figs. 1–8.

[60549] VGAM1820 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus. VGAM1820 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60550] VGAM1820 gene encodes a VGAM1820 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1820 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1820 precursor RNA is designated SEQ ID:1806, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1806 is located at position 7825 relative to the genome of Cryphonectria Hypovirus.

[60551] VGAM1820 precursor RNA folds onto itself, forming VGAM1820 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60552] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1820 folded precursor RNA into VGAM1820 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1820 RNA is designated SEQ ID:4531, and is provided hereinbelow with reference to the sequence listing part.

[60553] VGAM1820 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1820 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1820 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-



ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[60554] VGAM1820 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1820 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1820 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1820 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1820 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[60555] The complementary binding of VGAM1820 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1820 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1820 host target RNA into VGAM1820 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60556] It is appreciated that VGAM1820 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1820 host target genes. The mRNA of each one of this plurality of VGAM1820 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1820 RNA, herein designated VGAM RNA, and which when bound by VGAM1820 RNA causes inhibition of translation of respective one or more VGAM1820 host target proteins.

[60557] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1820 gene, herein designated VGAM GENE, on one

or more VGAM1820 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60558] It is yet further appreciated that a function of VGAM1820 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus. Specific functions, and accordingly utilities, of VGAM1820 correlate with, and may be deduced from, the identity of the host target genes which VGAM1820 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60559] Nucleotide sequences of the VGAM1820 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1820 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1820 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1820 are further described hereinbelow with reference to Table 1.

[60560] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1820 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1820 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60561] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1820 gene, herein designated VGAM is inhibition of expression of VGAM1820 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1820 correlate with, and may be deduced from, the identity of the target genes which VGAM1820 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60562] Estrogen-related Receptor Beta Like 1 (ESRRBL1, Acces-

sion NM\_018010) is a VGAM1820 host target gene. ESR-RBL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ESRRBL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESRRBL1 BINDING SITE, designated SEQ ID:19743, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60563] A function of VGAM1820 is therefore inhibition of Estrogen-related Receptor Beta Like 1 (ESRRBL1, Accession NM\_018010). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESRRBL1. Fasciculation and Elongation Protein Zeta 1 (zygin I) (FEZ1, Accession NM\_022549) is another VGAM1820 host target gene. FEZ1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FEZ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FEZ1 BINDING SITE, designated SEQ ID:22878, to the nu-

cleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60564] Another function of VGAM1820 is therefore inhibition of Fasciculation and Elongation Protein Zeta 1 (zygin I) (FEZ1, Accession NM\_022549), a gene which Zygin 1; may have a role in axonal outgrowth; has similarity to C. elegans UNC-76. Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FEZ1. The function of FEZ1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM37. Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542) is another VGAM1820 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45220, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60565] Another function of VGAM1820 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. Homeo Box D4 (HOXD4, Accession NM\_014621) is another VGAM1820 host target gene. HOXD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXD4 BINDING SITE, designated SEQ ID:15982, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60566] Another function of VGAM1820 is therefore inhibition of Homeo Box D4 (HOXD4, Accession NM\_014621), a gene

which is part of a developmental regulatory system. Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXD4. The function of HOXD4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM330.

NKX3A (Accession NM\_006167) is another VGAM1820 host target gene. NKX3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NKX3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NKX3A BINDING SITE, designated SEQ ID:12827, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60567] Another function of VGAM1820 is therefore inhibition of NKX3A (Accession NM\_006167), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NKX3A. The function of NKX3A and its as-



sociation with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM481. Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM\_005063) is another VGAM1820 host target gene. SCD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCD BINDING SITE, designated SEQ ID:11491, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60568] Another function of VGAM1820 is therefore inhibition of Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM\_005063), a gene which functions in the synthesis of unsaturated fatty acids. Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCD. The function of SCD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM314. SMT3 Suppressor of Mif Two 3 Homolog 1

(yeast) (SMT3H1, Accession XM\_009805) is another VGAM1820 host target gene. SMT3H1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMT3H1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMT3H1 BINDING SITE, designated SEQ ID:30124, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60569] Another function of VGAM1820 is therefore inhibition of SMT3 Suppressor of Mif Two 3 Homolog 1 (yeast) (SMT3H1, Accession XM\_009805), a gene which is involved in the function and/or structure of the eukaryotic kinetochore. Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMT3H1. The function of SMT3H1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM119. Chromobox Homolog 3 (HP1 gamma homolog, Drosophila) (CBX3, Accession NM\_007276) is another VGAM1820 host target gene. CBX3 BINDING SITE1 and

CBX3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CBX3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBX3 BINDING SITE1 and CBX3 BINDING SITE2, designated SEQ ID:14141 and SEQ ID:18661 respectively, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60570] Another function of VGAM1820 is therefore inhibition of Chromobox Homolog 3 (HP1 gamma homolog, Drosophila) (CBX3, Accession NM\_007276). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX3. Chromosome Y Open Reading Frame 14 (CYorf14, Accession NM\_018542) is another VGAM1820 host target gene. CYorf14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYorf14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYorf14 BINDING SITE, designated SEQ ID:20613, to the nucleotide sequence of

VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60571] Another function of VGAM1820 is therefore inhibition of Chromosome Y Open Reading Frame 14 (CYorf14, Accession NM\_018542). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYorf14. DKFZP434I092 (Accession XM\_042042) is another VGAM1820 host target gene. DKFZP434I092 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434I092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I092 BINDING SITE, designated SEQ ID:33675, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60572] Another function of VGAM1820 is therefore inhibition of DKFZP434I092 (Accession XM\_042042). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I092. FLJ14827 (Accession NM\_032848) is another VGAM1820 host target gene. FLJ14827 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14827 BINDING SITE, designated SEQ ID:26642, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60573] Another function of VGAM1820 is therefore inhibition of FLJ14827 (Accession NM\_032848). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14827. KIAA0247 (Accession NM\_014734) is another VGAM1820 host target gene. KIAA0247 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0247 BINDING SITE, designated SEQ ID:16371, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60574] Another function of VGAM1820 is therefore inhibition of

KIAA0247 (Accession NM\_014734). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0247. KIAA0367 (Accession XM\_041018) is another VGAM1820 host target gene. KIAA0367 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0367, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0367 BINDING SITE, designated SEQ ID:33417, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60575] Another function of VGAM1820 is therefore inhibition of KIAA0367 (Accession XM\_041018). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0367. KIAA1040 (Accession XM\_051091) is another VGAM1820 host target gene. KIAA1040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1040 BINDING SITE, designated SEQ ID:35741, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60576] Another function of VGAM1820 is therefore inhibition of KIAA1040 (Accession XM\_051091). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1040. Phosphodiesterase 7B (PDE7B, Accession NM\_018945) is another VGAM1820 host target gene. PDE7B BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PDE7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE7B BINDING SITE, designated SEQ ID:21011, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60577] Another function of VGAM1820 is therefore inhibition of Phosphodiesterase 7B (PDE7B, Accession NM\_018945). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with PDE7B. LOC145134 (Accession XM\_096722) is another VGAM1820 host target gene. LOC145134 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145134 BINDING SITE, designated SEQ ID:40502, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60578] Another function of VGAM1820 is therefore inhibition of LOC145134 (Accession XM\_096722). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145134. LOC90246 (Accession XM\_030283) is another VGAM1820 host target gene. LOC90246 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90246, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90246 BINDING SITE, designated SEQ ID:31000, to the



nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60579] Another function of VGAM1820 is therefore inhibition of LOC90246 (Accession XM\_030283). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90246. LOC93097 (Accession XM\_049221) is another VGAM1820 host target gene. LOC93097 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93097, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93097 BINDING SITE, designated SEQ ID:35355, to the nucleotide sequence of VGAM1820 RNA, herein designated VGAM RNA, also designated SEQ ID:4531.

[60580] Another function of VGAM1820 is therefore inhibition of LOC93097 (Accession XM\_049221). Accordingly, utilities of VGAM1820 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93097. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1821 (VGAM1821) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60581] VGAM1821 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1821 was detected is described hereinabove with reference to Figs. 1–8.

[60582] VGAM1821 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1821 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60583] VGAM1821 gene encodes a VGAM1821 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1821 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1821 precursor RNA is designated SEQ ID:1807, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1807 is located at position 28943 relative to the genome of Variola Virus.

[60584] VGAM1821 precursor RNA folds onto itself, forming VGAM1821 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60585] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1821 folded precursor RNA into VGAM1821 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM1821 RNA is designated SEQ ID:4532, and is provided hereinbelow with reference to the sequence listing part.

[60586] VGAM1821 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1821 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1821 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[60587] VGAM1821 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1821 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1821 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1821 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1821 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60588] The complementary binding of VGAM1821 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1821 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1821 host target RNA into VGAM1821 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60589] It is appreciated that VGAM1821 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1821 host target genes. The mRNA of each one of this plurality of VGAM1821 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1821 RNA, herein designated VGAM RNA, and which when bound by VGAM1821 RNA causes inhibition of translation of respective one or more VGAM1821 host target proteins.

[60590] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1821 gene, herein designated VGAM GENE, on one or more VGAM1821 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60591] It is yet further appreciated that a function of VGAM1821 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1821 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1821 correlate with, and may be deduced from, the identity of the host

target genes which VGAM1821 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60592] Nucleotide sequences of the VGAM1821 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1821 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1821 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1821 are further described hereinbelow with reference to Table 1.

[60593] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1821 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1821 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60594] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1821 gene, herein designated VGAM is inhibition of expression of VGAM1821 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1821 correlate with, and may be deduced from, the identity of the target genes which VGAM1821

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60595] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM\_004776) is a VGAM1821 host target gene. B4GALT5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by B4GALT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT5 BINDING SITE, designated SEQ ID:11170, to the nucleotide sequence of VGAM1821 RNA, herein designated VGAM RNA, also designated SEQ ID:4532.

[60596] A function of VGAM1821 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM\_004776). Accordingly, utilities of VGAM1821 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT5. BCL2-antagonist/killer 1 (BAK1, Accession XM\_166333) is another VGAM1821 host target gene. BAK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BAK1, corresponding to a HOST TARGET binding site such as



BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAK1 BINDING SITE, designated SEQ ID:44175, to the nucleotide sequence of VGAM1821 RNA, herein designated VGAM RNA, also designated SEQ ID:4532.

[60597] Another function of VGAM1821 is therefore inhibition of BCL2-antagonist/killer 1 (BAK1, Accession XM\_166333), a gene which accelerates programmed cell death by binding to, and antagonizing the a repressor bcl-2. Accordingly, utilities of VGAM1821 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAK1. The function of BAK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430.Forkhead Box O1A

(rhabdomyosarcoma) (FOXO1A, Accession NM\_002015) is another VGAM1821 host target gene. FOXO1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FOXO1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXO1A BINDING SITE, designated SEQ ID:7758, to the

nucleotide sequence of VGAM1821 RNA, herein designated VGAM RNA, also designated SEQ ID:4532.

[60598] Another function of VGAM1821 is therefore inhibition of Forkhead Box O1A (rhabdomyosarcoma) (FOXO1A, Accession NM\_002015), a gene which is a probable transcription factor. Accordingly, utilities of VGAM1821 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXO1A. The function of FOXO1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM228. Angiomotin Like 2 (AMOTL2, Accession NM\_016201) is another VGAM1821 host target gene. AMOTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMOTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOTL2 BINDING SITE, designated SEQ ID:18293, to the nucleotide sequence of VGAM1821 RNA, herein designated VGAM RNA, also designated SEQ ID:4532.

[60599] Another function of VGAM1821 is therefore inhibition of

Angiomotin Like 2 (AMOTL2, Accession NM\_016201). Accordingly, utilities of VGAM1821 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOTL2. FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM\_054016) is another VGAM1821 host target gene. FUSIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUSIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUSIP1 BINDING SITE, designated SEQ ID:27624, to the nucleotide sequence of VGAM1821 RNA, herein designated VGAM RNA, also designated SEQ ID:4532.

[60600] Another function of VGAM1821 is therefore inhibition of FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM\_054016). Accordingly, utilities of VGAM1821 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUSIP1. MGC10999 (Accession NM\_032307) is another VGAM1821 host target gene. MGC10999 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10999, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10999 BINDING SITE, designated SEQ ID:26090, to the nucleotide sequence of VGAM1821 RNA, herein designated VGAM RNA, also designated SEQ ID:4532.

[60601] Another function of VGAM1821 is therefore inhibition of MGC10999 (Accession NM\_032307). Accordingly, utilities of VGAM1821 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10999. LOC153259 (Accession XM\_098342) is another VGAM1821 host target gene. LOC153259 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153259, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153259 BINDING SITE, designated SEQ ID:41600, to the nucleotide sequence of VGAM1821 RNA, herein designated VGAM RNA, also designated SEQ ID:4532.

[60602] Another function of VGAM1821 is therefore inhibition of LOC153259 (Accession XM\_098342). Accordingly, utilities of VGAM1821 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC153259. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1822 (VGAM1822) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60603] VGAM1822 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1822 was detected is described hereinabove with reference to Figs. 1–8.

[60604] VGAM1822 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus. VGAM1822 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60605] VGAM1822 gene encodes a VGAM1822 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1822 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1822 precursor RNA is desig-

nated SEQ ID:1808, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1808 is located at position 9148 relative to the genome of Cryphonectria Hypovirus.

[60606] VGAM1822 precursor RNA folds onto itself, forming VGAM1822 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60607] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1822 folded precursor RNA into VGAM1822 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1822 RNA is designated SEQ ID:4533, and is provided hereinbelow with reference to the sequence

listing part.

[60608] VGAM1822 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1822 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1822 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60609] VGAM1822 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1822 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1822 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1822 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1822 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60610] The complementary binding of VGAM1822 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1822 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1822 host target RNA into VGAM1822 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60611] It is appreciated that VGAM1822 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1822 host target genes. The mRNA of each one of this plurality of VGAM1822 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1822 RNA, herein designated VGAM



RNA, and which when bound by VGAM1822 RNA causes inhibition of translation of respective one or more VGAM1822 host target proteins.

[60612] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1822 gene, herein designated VGAM GENE, on one or more VGAM1822 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60613] It is yet further appreciated that a function of VGAM1822 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1822 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus. Specific functions, and accordingly utilities, of VGAM1822 correlate with, and may be deduced from, the identity of the host target genes which VGAM1822 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60614] Nucleotide sequences of the VGAM1822 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1822 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1822 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1822 are further described hereinbelow with reference to Table 1.

[60615] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1822 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1822 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60616] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1822 gene, herein designated VGAM is

inhibition of expression of VGAM1822 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1822 correlate with, and may be deduced from, the identity of the target genes which VGAM1822 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60617] MEP50 (Accession NM\_024102) is a VGAM1822 host target gene. MEP50 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEP50, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEP50 BINDING SITE, designated SEQ ID:23548, to the nucleotide sequence of VGAM1822 RNA, herein designated VGAM RNA, also designated SEQ ID:4533.

[60618] A function of VGAM1822 is therefore inhibition of MEP50 (Accession NM\_024102). Accordingly, utilities of VGAM1822 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEP50. LOC139197 (Accession XM\_066541) is another VGAM1822 host target gene. LOC139197 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC139197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139197 BINDING SITE, designated SEQ ID:37329, to the nucleotide sequence of VGAM1822 RNA, herein designated VGAM RNA, also designated SEQ ID:4533.

[60619] Another function of VGAM1822 is therefore inhibition of LOC139197 (Accession XM\_066541). Accordingly, utilities of VGAM1822 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139197. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1823 (VGAM1823) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60620] VGAM1823 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1823 was detected is described hereinabove with reference to Figs. 1-8.

[60621] VGAM1823 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Cryphonectria Hypovirus. VGAM1823 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60622] VGAM1823 gene encodes a VGAM1823 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1823 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1823 precursor RNA is designated SEQ ID:1809, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1809 is located at position 3317 relative to the genome of Cryphonectria Hypovirus.

[60623] VGAM1823 precursor RNA folds onto itself, forming VGAM1823 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60624] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1823 folded precursor RNA into VGAM1823 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1823 RNA is designated SEQ ID:4534, and is provided hereinbelow with reference to the sequence listing part.

[60625] VGAM1823 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1823 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1823 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60626] VGAM1823 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1823 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1823 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1823 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1823 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60627] The complementary binding of VGAM1823 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1823 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1823

host target RNA into VGAM1823 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60628] It is appreciated that VGAM1823 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1823 host target genes. The mRNA of each one of this plurality of VGAM1823 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1823 RNA, herein designated VGAM RNA, and which when bound by VGAM1823 RNA causes inhibition of translation of respective one or more VGAM1823 host target proteins.

[60629] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1823 gene, herein designated VGAM GENE, on one or more VGAM1823 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60630] It is yet further appreciated that a function of VGAM1823 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1823 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus. Specific functions, and accordingly utilities, of VGAM1823 correlate with, and may be deduced from, the identity of the host target genes which VGAM1823 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60631] Nucleotide sequences of the VGAM1823 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1823 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1823 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1823 are further

described hereinbelow with reference to Table 1.

[60632] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1823 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1823 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60633] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1823 gene, herein designated VGAM is inhibition of expression of VGAM1823 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1823 correlate with, and may be deduced from, the identity of the target genes which VGAM1823 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60634] KIAA0547 (Accession NM\_014793) is a VGAM1823 host target gene. KIAA0547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0547 BINDING SITE,

designated SEQ ID:16693, to the nucleotide sequence of VGAM1823 RNA, herein designated VGAM RNA, also designated SEQ ID:4534.

[60635] A function of VGAM1823 is therefore inhibition of KIAA0547 (Accession NM\_014793). Accordingly, utilities of VGAM1823 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0547. NDP52 (Accession NM\_005831) is another VGAM1823 host target gene. NDP52 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDP52, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDP52 BINDING SITE, designated SEQ ID:12446, to the nucleotide sequence of VGAM1823 RNA, herein designated VGAM RNA, also designated SEQ ID:4534.

[60636] Another function of VGAM1823 is therefore inhibition of NDP52 (Accession NM\_005831). Accordingly, utilities of VGAM1823 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDP52. Oxysterol Binding Protein-like 2 (OSBPL2, Accession NM\_014835) is another VGAM1823 host target gene. OS-

BPL2 BINDING SITE1 and OSBPL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OSBPL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL2 BINDING SITE1 and OSBPL2 BINDING SITE2, designated SEQ ID:16847 and SEQ ID:29315 respectively, to the nucleotide sequence of VGAM1823 RNA, herein designated VGAM RNA, also designated SEQ ID:4534.

[60637] Another function of VGAM1823 is therefore inhibition of Oxysterol Binding Protein-like 2 (OSBPL2, Accession NM\_014835). Accordingly, utilities of VGAM1823 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL2. LOC197358 (Accession XM\_113872) is another VGAM1823 host target gene. LOC197358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197358 BINDING SITE, designated SEQ ID:42509, to the nucleotide sequence of

VGAM1823 RNA, herein designated VGAM RNA, also designated SEQ ID:4534.

[60638] Another function of VGAM1823 is therefore inhibition of LOC197358 (Accession XM\_113872). Accordingly, utilities of VGAM1823 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197358. LOC200317 (Accession XM\_114208) is another VGAM1823 host target gene. LOC200317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200317 BINDING SITE, designated SEQ ID:42803, to the nucleotide sequence of VGAM1823 RNA, herein designated VGAM RNA, also designated SEQ ID:4534.

[60639] Another function of VGAM1823 is therefore inhibition of LOC200317 (Accession XM\_114208). Accordingly, utilities of VGAM1823 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200317. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1824 (VGAM1824) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60640] VGAM1824 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1824 was detected is described hereinabove with reference to Figs. 1–8.

[60641] VGAM1824 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus. VGAM1824 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60642] VGAM1824 gene encodes a VGAM1824 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1824 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1824 precursor RNA is designated SEQ ID:1810, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1810 is located at position 3901 relative to the genome of Cryphonectria Hypovirus.

[60643] VGAM1824 precursor RNA folds onto itself, forming VGAM1824 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60644] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1824 folded precursor RNA into VGAM1824 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1824 RNA is designated SEQ ID:4535, and is provided hereinbelow with reference to the sequence listing part.

[60645] VGAM1824 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1824 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1824 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[60646] VGAM1824 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1824 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1824 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1824 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1824 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding



sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60647] The complementary binding of VGAM1824 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1824 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1824 host target RNA into VGAM1824 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60648] It is appreciated that VGAM1824 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1824 host target genes. The mRNA of each one of this plurality of VGAM1824 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1824 RNA, herein designated VGAM RNA, and which when bound by VGAM1824 RNA causes inhibition of translation of respective one or more VGAM1824 host target proteins.

[60649] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1824 gene, herein designated VGAM GENE, on one or more VGAM1824 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60650] It is yet further appreciated that a function of VGAM1824 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1824 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus. Specific functions, and accordingly utilities, of VGAM1824 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1824 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60651] Nucleotide sequences of the VGAM1824 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1824 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1824 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1824 are further described hereinbelow with reference to Table 1.

[60652] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1824 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1824 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60653] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1824 gene, herein designated VGAM is inhibition of expression of VGAM1824 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1824 correlate with, and may be deduced from, the identity of the target genes which VGAM1824

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60654] FLJ21032 (Accession NM\_024906) is a VGAM1824 host target gene. FLJ21032 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ21032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21032 BINDING SITE, designated SEQ ID:24395, to the nucleotide sequence of VGAM1824 RNA, herein designated VGAM RNA, also designated SEQ ID:4535.

[60655] A function of VGAM1824 is therefore inhibition of FLJ21032 (Accession NM\_024906). Accordingly, utilities of VGAM1824 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21032. KIAA0258 (Accession NM\_014785) is another VGAM1824 host target gene. KIAA0258 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0258 BINDING SITE, designated SEQ ID:16642, to the nucleotide sequence of VGAM1824 RNA, herein designated VGAM RNA, also designated SEQ ID:4535.

[60656] Another function of VGAM1824 is therefore inhibition of KIAA0258 (Accession NM\_014785). Accordingly, utilities of VGAM1824 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0258. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1825 (VGAM1825) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60657] VGAM1825 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1825 was detected is described hereinabove with reference to Figs. 1–8.

[60658] VGAM1825 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia Virus. VGAM1825 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60659] VGAM1825 gene encodes a VGAM1825 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1825 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1825 precursor RNA is designated SEQ ID:1811, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1811 is located at position 34526 relative to the genome of Vaccinia Virus.

[60660] VGAM1825 precursor RNA folds onto itself, forming VGAM1825 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60661] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1825 folded precursor RNA into VGAM1825 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM1825 RNA is designated SEQ ID:4536, and is provided hereinbelow with reference to the sequence listing part.

[60662] VGAM1825 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1825 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1825 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60663] VGAM1825 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1825 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1825 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1825 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1825 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60664] The complementary binding of VGAM1825 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1825 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1825 host target RNA into VGAM1825 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60665] It is appreciated that VGAM1825 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1825 host target genes. The mRNA of each one of this plurality of VGAM1825 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1825 RNA, herein designated VGAM RNA, and which when bound by VGAM1825 RNA causes inhibition of translation of respective one or more VGAM1825 host target proteins.

[60666] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1825 gene, herein designated VGAM GENE, on one or more VGAM1825 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[60667] It is yet further appreciated that a function of VGAM1825 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1825 include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGAM1825 correlate with, and may be deduced from, the identity of the host target genes which VGAM1825 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60668] Nucleotide sequences of the VGAM1825 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1825 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1825 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1825 are further described hereinbelow with reference to Table 1.

[60669] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1825 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1825 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60670] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1825 gene, herein designated VGAM is inhibition of expression of VGAM1825 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1825 correlate with, and may be deduced from, the identity of the target genes which VGAM1825 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60671] RAS P21 Protein Activator (GTPase activating protein) 1 (RASA1, Accession NM\_022650) is a VGAM1825 host target gene. RASA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASA1 BINDING SITE, designated SEQ ID:22907, to the nucleotide sequence of VGAM1825 RNA, herein designated VGAM RNA, also designated SEQ ID:4536.

[60672] A function of VGAM1825 is therefore inhibition of RAS P21 Protein Activator (GTPase activating protein) 1 (RASA1, Accession NM\_022650), a gene which is involved in the control of cellular proliferation and differentiation. Accordingly, utilities of VGAM1825 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASA1. The function of RASA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM464.Selenoprotein P, Plasma, 1 (SEPP1, Accession NM\_005410) is another VGAM1825 host target gene. SEPP1 BINDING SITE1 and SEPP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SEPP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPP1 BINDING SITE1 and SEPP1 BINDING SITE2, designated SEQ ID:11878 and SEQ ID:30185 respectively, to the nucleotide sequence of VGAM1825 RNA, herein designated VGAM RNA, also designated SEQ ID:4536.

[60673] Another function of VGAM1825 is therefore inhibition of

Selenoprotein P, Plasma, 1 (SEPP1, Accession NM\_005410), a gene which might be responsible for some of the extracellular antioxidant defense properties of selenium or might be involved in the transport of selenium. Accordingly, utilities of VGAM1825 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPP1. The function of SEPP1 has been established by previous studies. Selenium is an essential trace element that is incorporated as selenocysteine into the primary structure of selenoproteins. There are at least 10 animal selenoproteins. Nutritional deficiency of selenium decreases selenoprotein concentrations and leads to pathologic conditions. Human populations that are selenium deficient are susceptible to the development of Keshan disease, a cardiomyopathy of children reported in selenium-deficient areas of China (Keshan Disease Research Group of the Chinese Academy of Medical Sciences, 1979). Hill et al. (1996) cited animal studies that have demonstrated roles for selenium in oxidant defense, thyroid hormone metabolism, and defense against viral infections. Selenoproteins presumably mediate these biologic effects. Human selenoproteins include glutathione peroxidase-1 (OMIM Ref. No. 138320), thiore-

doxin reductase (OMIM Ref. No. 601112), glutathione peroxidase-2 (OMIM Ref. No. 138319), glutathione peroxidase-3 (OMIM Ref. No. 138321), thyroxine deiodinase type 1 (OMIM Ref. No. 147892), and mitochondrial capsule selenoprotein (OMIM Ref. No. 601148). Most of the known selenoproteins are members of the glutathione peroxidase or iodothyronine deiodinase families. Hill et al. (1996) stated that selenoprotein P (SEPP1) is a major selenoprotein that is not a member of those families. It is an extracellular glycoprotein that is present in several isoforms and is the only selenoprotein known to contain multiple selenocysteine residues (Hill et al., 1993). It is a heparin-binding protein that appears to be associated with endothelial cells and has been implicated as an oxidant defense in the extracellular space. Hill et al. (1993) cloned human selenoprotein P from a liver cDNA library. The human open reading frame is 69% identical to that of rat selenoprotein P and the predicted proteins share 72% amino acid identity. Hill et al. (1996) mapped the SEPP1 gene to chromosome 5 by Southern analysis of 2 somatic cell hybrid DNA panels using as a probe their liver cDNA library clone. They narrowed the assignment to 5q31 by fluorescence in situ hybridization. Only 1 SEPP1 locus was

detected. Although there is evidence of several isoforms of the protein, all of them share the same N-terminal sequence and therefore are likely products of the same gene (Chittum et al., 1996). Hill et al. (1996) commented that limb-girdle muscular dystrophy type 1A(LGMD1A; 159000) maps to the distal portion of 5q. They noted that since selenium deficiency is associated with nutritional muscular dystrophies in several species, it might be of interest to evaluate SEPP1 in that form of muscular dystrophy. Acute nonlymphocytic leukemia and the myelodysplastic syndrome are associated with deletions of a critical region of 5q.

[60674] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[60675] Hill, K. E.; Dasouki, M.; Phillips, J. A., III; Burk, R. F. : Human selenoprotein P gene maps to 5q31. *Genomics* 36: 550–551, 1996. ; and

[60676] Hill, K. E.; Lloyd, R. S.; Burk, R. F. : Conserved nucleotide sequences in the open reading frame and 3-prime untranslated region of selenoprotein P mRNA. *Proc. Nat. Acad. Sci.* 90: 537–5.

[60677] Further studies establishing the function and utilities of

SEPP1 are found in John Hopkins OMIM database record ID 601484, and in cited publications numbered 7028–6830 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fatty Acid Desaturase 1 (FADS1, Accession NM\_013402) is another VGAM1825 host target gene. FADS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FADS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FADS1 BINDING SITE, designated SEQ ID:15067, to the nucleotide sequence of VGAM1825 RNA, herein designated VGAM RNA, also designated SEQ ID:4536.

[60678] Another function of VGAM1825 is therefore inhibition of Fatty Acid Desaturase 1 (FADS1, Accession NM\_013402). Accordingly, utilities of VGAM1825 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FADS1. GENX-3414 (Accession NM\_003943) is another VGAM1825 host target gene. GENX-3414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GENX-3414, corresponding to a HOST TARGET binding



site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GENX-3414 BINDING SITE, designated SEQ ID:10059, to the nucleotide sequence of VGAM1825 RNA, herein designated VGAM RNA, also designated SEQ ID:4536.

[60679] Another function of VGAM1825 is therefore inhibition of GENX-3414 (Accession NM\_003943). Accordingly, utilities of VGAM1825 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GENX-3414. MGC3048 (Accession NM\_024052) is another VGAM1825 host target gene. MGC3048 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3048, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3048 BINDING SITE, designated SEQ ID:23488, to the nucleotide sequence of VGAM1825 RNA, herein designated VGAM RNA, also designated SEQ ID:4536.

[60680] Another function of VGAM1825 is therefore inhibition of MGC3048 (Accession NM\_024052). Accordingly, utilities of VGAM1825 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC3048. YME1-like 1 (*S. cerevisiae*) (YME1L1, Accession NM\_139312) is another VGAM1825 host target gene. YME1L1 BINDING SITE1 and YME1L1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by YME1L1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YME1L1 BINDING SITE1 and YME1L1 BINDING SITE2, designated SEQ ID:29293 and SEQ ID:15537 respectively, to the nucleotide sequence of VGAM1825 RNA, herein designated VGAM RNA, also designated SEQ ID:4536.

[60681] Another function of VGAM1825 is therefore inhibition of YME1-like 1 (*S. cerevisiae*) (YME1L1, Accession NM\_139312). Accordingly, utilities of VGAM1825 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YME1L1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1826 (VGAM1826) viral gene, which modulates expression of respective host target genes thereof, the function and

utility of which host target genes is known in the art.

[60682] VGAM1826 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1826 was detected is described hereinabove with reference to Figs. 1–8.

[60683] VGAM1826 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1826 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60684] VGAM1826 gene encodes a VGAM1826 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1826 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1826 precursor RNA is designated SEQ ID:1812, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1812 is located at position 29285 relative to the genome of Variola Virus.

[60685] VGAM1826 precursor RNA folds onto itself, forming VGAM1826 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60686] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1826 folded precursor RNA into VGAM1826 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1826 RNA is designated SEQ ID:4537, and is provided hereinbelow with reference to the sequence listing part.

[60687] VGAM1826 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1826 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1826 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[60688] VGAM1826 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1826 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1826 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1826 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1826 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[60689] The complementary binding of VGAM1826 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1826 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1826 host target RNA into VGAM1826 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60690] It is appreciated that VGAM1826 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1826 host target genes. The mRNA of each one of this plurality of VGAM1826 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1826 RNA, herein designated VGAM RNA, and which when bound by VGAM1826 RNA causes inhibition of translation of respective one or more VGAM1826 host target proteins.

[60691] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1826 gene, herein designated VGAM GENE, on one

or more VGAM1826 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60692] It is yet further appreciated that a function of VGAM1826 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1826 correlate with, and may be deduced from, the identity of the host target genes which VGAM1826 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60693] Nucleotide sequences of the VGAM1826 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1826 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1826 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1826 are further described hereinbelow with reference to Table 1.

[60694] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1826 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1826 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60695] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1826 gene, herein designated VGAM is inhibition of expression of VGAM1826 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1826 correlate with, and may be deduced from, the identity of the target genes which VGAM1826 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60696] Cyclin D2 (CCND2, Accession NM\_001759) is a VGAM1826



host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7512, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60697] A function of VGAM1826 is therefore inhibition of Cyclin D2 (CCND2, Accession NM\_001759), a gene which is essential for the control of the cell cycle at the g1/s (start) transition. Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128. Hyaluronan Synthase 2 (HAS2, Accession NM\_005328) is another VGAM1826 host target gene. HAS2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HAS2, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HAS2 BINDING SITE, designated SEQ ID:11801, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60698] Another function of VGAM1826 is therefore inhibition of Hyaluronan Synthase 2 (HAS2, Accession NM\_005328), a gene which plays a role in hyaluronan/hyaluronic acid (ha) synthesis and transport . Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HAS2. The function of HAS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM874. Integrin, Beta-like 1 (with EGF-like repeat domains) (ITGBL1, Accession NM\_004791) is another VGAM1826 host target gene. ITGBL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGBL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGBL1 BINDING SITE, designated SEQ ID:11201, to the nucleotide se-

quence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60699] Another function of VGAM1826 is therefore inhibition of Integrin, Beta-like 1 (with EGF-like repeat domains) (ITGBL1, Accession NM\_004791). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGBL1. Neurofilament, Heavy Polypeptide 200kDa (NEFH, Accession NM\_021076) is another VGAM1826 host target gene. NEFH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEFH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEFH BINDING SITE, designated SEQ ID:22046, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60700] Another function of VGAM1826 is therefore inhibition of Neurofilament, Heavy Polypeptide 200kDa (NEFH, Accession NM\_021076), a gene which is involved in the maintenance of neuronal caliber and in mature axons. Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with NEFH. The function of NEFH has been established by previous studies. See 162280. Mattei et al. (1988) used a rat cDNA probe coding for the C-terminal extension of the NFH gene to assign, by in situ hybridization, the human NFH gene to 22q12.1-q13.1. The possible implications of the fact that neurologic disorders such as meningioma map to this region were discussed. In the course of cloning the region between 2 markers, D22S212 and D22S32, that flank the NF2 (OMIM Ref. No. 101000) gene, Rouleau et al. (1993) identified a gene with a neuronal pattern of expression and a transcript size identical to that of NEFH. Use of NEFH cDNA confirmed the identity. There is compelling evidence that the NEFH locus is close to the NF2 locus. For example, Watson et al. (1993) found that the NEFH locus was hemizygous in a deletion that was observed in affected members of a family with NF2 and was estimated to be about 700 kb long. The NF2 locus has been positioned at 22q12.2. Bucan et al. (1993) mapped the homologous murine gene, which they symbolized *Nfh*, to chromosome 11. The tail of the heavy neurofilament subunit is composed of the repeating amino acid motif, usually X-ly-sine-serine-proline-Y-lysine (OMIM Ref. No. XKSPYK),

where X is a single amino acid and Y is 1 to 3 amino acids. There are 2 common polymorphic variants of 44 and 45 repeats. The tail probably regulates axonal caliber, with interfilament spacing determined by phosphorylation of the KSP motifs. According to Al-Chalabi et al. (1999), the polymorphic variants had been mislabeled in the published literature as 44 and 43 repeat variants, respectively, and therefore were referred to by them simply as long (L) and short (S) alleles.

[60701] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[60702] Al-Chalabi, A.; Andersen, P. M.; Nilsson, P.; Chioza, B.; Andersson, J. L.; Russ, C.; Shaw, C. E.; Powell, J. F.; Leigh, P. N. : Deletions of the heavy neurofilament subunit tail in amyotrophic lateral sclerosis. Hum. Molec. Genet. 8: 157–164, 1999. ; and

[60703] Watson, C. J.; Gaunt, L.; Evans, G.; Patel, K.; Harris, R.; Strachan, T. : A disease-associated germline deletion maps the type 2 neurofibromatosis (NF2) gene between the Ewing sarcoma.

[60704] Further studies establishing the function and utilities of NEFH are found in John Hopkins OMIM database record ID

162230, and in cited publications numbered 1029 and 10293–10301 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 22 Open Reading Frame 5 (C22orf5, Accession NM\_012264) is another VGAM1826 host target gene. C22orf5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C22orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf5 BINDING SITE, designated SEQ ID:14585, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60705] Another function of VGAM1826 is therefore inhibition of Chromosome 22 Open Reading Frame 5 (C22orf5, Accession NM\_012264). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf5. Centaurin, Beta 5 (CENTB5, Accession XM\_170937) is another VGAM1826 host target gene. CENTB5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CENTB5, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTB5 BINDING SITE, designated SEQ ID:45723, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60706] Another function of VGAM1826 is therefore inhibition of Centaurin, Beta 5 (CENTB5, Accession XM\_170937). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTB5. FLJ00026 (Accession XM\_036307) is another VGAM1826 host target gene. FLJ00026 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ00026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00026 BINDING SITE, designated SEQ ID:32427, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60707] Another function of VGAM1826 is therefore inhibition of FLJ00026 (Accession XM\_036307). Accordingly, utilities of

VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00026. FLJ10718 (Accession NM\_018192) is another VGAM1826 host target gene. FLJ10718 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10718, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10718 BINDING SITE, designated SEQ ID:20048, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60708] Another function of VGAM1826 is therefore inhibition of FLJ10718 (Accession NM\_018192). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10718. FLJ10743 (Accession NM\_018201) is another VGAM1826 host target gene. FLJ10743 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10743



BINDING SITE, designated SEQ ID:20081, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60709] Another function of VGAM1826 is therefore inhibition of FLJ10743 (Accession NM\_018201). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10743. FLJ14260 (Accession NM\_025027) is another VGAM1826 host target gene. FLJ14260 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14260, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14260 BINDING SITE, designated SEQ ID:24618, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60710] Another function of VGAM1826 is therefore inhibition of FLJ14260 (Accession NM\_025027). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14260. FLJ14800 (Accession NM\_032840) is another VGAM1826 host target gene. FLJ14800 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14800 BINDING SITE, designated SEQ ID:26620, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60711] Another function of VGAM1826 is therefore inhibition of FLJ14800 (Accession NM\_032840). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14800. FLJ14810 (Accession NM\_032843) is another VGAM1826 host target gene. FLJ14810 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14810, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14810 BINDING SITE, designated SEQ ID:26631, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60712] Another function of VGAM1826 is therefore inhibition of

FLJ14810 (Accession NM\_032843). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14810. FLJ20079 (Accession NM\_017656) is another VGAM1826 host target gene. FLJ20079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19172, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60713] Another function of VGAM1826 is therefore inhibition of FLJ20079 (Accession NM\_017656). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. FLJ30294 (Accession NM\_144632) is another VGAM1826 host target gene. FLJ30294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ30294 BINDING SITE, designated SEQ ID:29449, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60714] Another function of VGAM1826 is therefore inhibition of FLJ30294 (Accession NM\_144632). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30294. KIAA0430 (Accession NM\_019081) is another VGAM1826 host target gene. KIAA0430 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0430 BINDING SITE, designated SEQ ID:21152, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60715] Another function of VGAM1826 is therefore inhibition of KIAA0430 (Accession NM\_019081). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0430. KIAA0564 (Accession XM\_038664) is another

VGAM1826 host target gene. KIAA0564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0564 BINDING SITE, designated SEQ ID:32900, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60716] Another function of VGAM1826 is therefore inhibition of KIAA0564 (Accession XM\_038664). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0564. MGC15882 (Accession NM\_032884) is another VGAM1826 host target gene. MGC15882 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15882, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15882 BINDING SITE, designated SEQ ID:26706, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60717] Another function of VGAM1826 is therefore inhibition of MGC15882 (Accession NM\_032884). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15882. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM\_004263) is another VGAM1826 host target gene. SEMA4F BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA4F, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4F BINDING SITE, designated SEQ ID:10460, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60718] Another function of VGAM1826 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM\_004263). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4F. Sialyltransferase 4A

(beta-galactoside alpha-2,3-sialyltransferase) (SIAT4A, Accession NM\_003033) is another VGAM1826 host target gene. SIAT4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIAT4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT4A BINDING SITE, designated SEQ ID:8978, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60719] Another function of VGAM1826 is therefore inhibition of Sialyltransferase 4A (beta-galactoside alpha-2,3-sialyltransferase) (SIAT4A, Accession NM\_003033). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT4A. VEZATIN (Accession NM\_017599) is another VGAM1826 host target gene. VEZATIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VEZATIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of VEZATIN BINDING SITE, designated SEQ ID:19068, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60720] Another function of VGAM1826 is therefore inhibition of VEZATIN (Accession NM\_017599). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VEZATIN. LOC120087 (Accession XM\_061853) is another VGAM1826 host target gene. LOC120087 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC120087, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120087 BINDING SITE, designated SEQ ID:37208, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60721] Another function of VGAM1826 is therefore inhibition of LOC120087 (Accession XM\_061853). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120087. LOC138128 (Accession XM\_070769) is an-



other VGAM1826 host target gene. LOC138128 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC138128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138128 BINDING SITE, designated SEQ ID:37393, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60722] Another function of VGAM1826 is therefore inhibition of LOC138128 (Accession XM\_070769). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138128. LOC148930 (Accession XM\_086369) is another VGAM1826 host target gene. LOC148930 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC148930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148930 BINDING SITE, designated SEQ ID:38616, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60723] Another function of VGAM1826 is therefore inhibition of LOC148930 (Accession XM\_086369). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148930. LOC150372 (Accession XM\_086893) is another VGAM1826 host target gene. LOC150372 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150372, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150372 BINDING SITE, designated SEQ ID:38936, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60724] Another function of VGAM1826 is therefore inhibition of LOC150372 (Accession XM\_086893). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150372. LOC151877 (Accession XM\_098132) is another VGAM1826 host target gene. LOC151877 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151877, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151877 BINDING SITE, designated SEQ ID:41393, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60725] Another function of VGAM1826 is therefore inhibition of LOC151877 (Accession XM\_098132). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151877. LOC154761 (Accession XM\_088038) is another VGAM1826 host target gene. LOC154761 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154761 BINDING SITE, designated SEQ ID:39483, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60726] Another function of VGAM1826 is therefore inhibition of LOC154761 (Accession XM\_088038). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC154761. LOC163882 (Accession XM\_089211) is another VGAM1826 host target gene. LOC163882 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC163882, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163882 BINDING SITE, designated SEQ ID:39973, to the nucleotide sequence of VGAM1826 RNA, herein designated VGAM RNA, also designated SEQ ID:4537.

[60727] Another function of VGAM1826 is therefore inhibition of LOC163882 (Accession XM\_089211). Accordingly, utilities of VGAM1826 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163882. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1827 (VGAM1827) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60728] VGAM1827 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1827 was detected is described hereinabove with reference to Figs. 1–8.

[60729] VGAM1827 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM1827 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60730] VGAM1827 gene encodes a VGAM1827 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1827 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1827 precursor RNA is designated SEQ ID:1813, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1813 is located at position 144104 relative to the genome of Rabbit Fibroma Virus.

[60731] VGAM1827 precursor RNA folds onto itself, forming VGAM1827 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60732] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1827 folded precursor RNA into VGAM1827 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1827 RNA is designated SEQ ID:4538, and is provided hereinbelow with reference to the sequence listing part.

[60733] VGAM1827 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1827 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1827 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60734] VGAM1827 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1827 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1827 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1827 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1827 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[60735] The complementary binding of VGAM1827 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1827 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1827 host target RNA into VGAM1827 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60736] It is appreciated that VGAM1827 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1827 host target genes. The mRNA of each one of this plurality of VGAM1827 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1827 RNA, herein designated VGAM RNA, and which when bound by VGAM1827 RNA causes inhibition of translation of respective one or more VGAM1827 host target proteins.

[60737] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1827 gene, herein designated VGAM GENE, on one or more VGAM1827 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60738] It is yet further appreciated that a function of VGAM1827 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1827 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM1827 correlate with, and may be deduced from, the identity of the host target genes which VGAM1827 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60739] Nucleotide sequences of the VGAM1827 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1827 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1827 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1827 are further described hereinbelow with reference to Table 1.

[60740] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1827 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1827 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60741] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1827 gene, herein designated VGAM is inhibition of expression of VGAM1827 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1827 correlate with, and may be deduced from, the identity of the target genes which VGAM1827 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60742] SE57-1 (Accession NM\_025214) is a VGAM1827 host target gene. SE57-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SE57-1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SE57-1 BINDING SITE, designated SEQ ID:24886, to the nucleotide sequence of VGAM1827 RNA, herein designated VGAM RNA, also designated SEQ ID:4538.

[60743] A function of VGAM1827 is therefore inhibition of SE57-1 (Accession NM\_025214). Accordingly, utilities of VGAM1827 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SE57-1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1828 (VGAM1828) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60744] VGAM1828 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1828 was detected is described hereinabove with reference to Figs. 1-8.

[60745] VGAM1828 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus.

VGAM1828 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60746] VGAM1828 gene encodes a VGAM1828 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1828 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1828 precursor RNA is designated SEQ ID:1814, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1814 is located at position 140535 relative to the genome of Rabbit Fibroma Virus.

[60747] VGAM1828 precursor RNA folds onto itself, forming VGAM1828 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60748] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1828 folded precursor RNA into VGAM1828 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1828 RNA is designated SEQ ID:4539, and is provided hereinbelow with reference to the sequence listing part.

[60749] VGAM1828 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1828 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1828 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60750] VGAM1828 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1828 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1828 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1828 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1828 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60751] The complementary binding of VGAM1828 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1828 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1828 host target RNA into VGAM1828 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60752] It is appreciated that VGAM1828 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1828 host target genes. The mRNA of each one of this plurality of VGAM1828 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1828 RNA, herein designated VGAM RNA, and which when bound by VGAM1828 RNA causes inhibition of translation of respective one or more VGAM1828 host target proteins.

[60753] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1828 gene, herein designated VGAM GENE, on one or more VGAM1828 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60754] It is yet further appreciated that a function of VGAM1828 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1828 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM1828 correlate with, and may be deduced from, the identity of the host target genes which VGAM1828 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60755] Nucleotide sequences of the VGAM1828 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1828 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1828 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1828 are further described hereinbelow with reference to Table 1.



[60756] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1828 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1828 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60757] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1828 gene, herein designated VGAM is inhibition of expression of VGAM1828 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1828 correlate with, and may be deduced from, the identity of the target genes which VGAM1828 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60758] Transducin (beta)-like 1X-linked (TBL1X, Accession NM\_005647) is a VGAM1828 host target gene. TBL1X BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBL1X, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBL1X BINDING SITE, designated SEQ ID:12184, to the

nucleotide sequence of VGAM1828 RNA, herein designated VGAM RNA, also designated SEQ ID:4539.

[60759] A function of VGAM1828 is therefore inhibition of Transducin (beta)-like 1X-linked (TBL1X, Accession NM\_005647), a gene which activates latent HDAC3 activity. Accordingly, utilities of VGAM1828 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBL1X. The function of TBL1X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1151. Chromosome X Open Reading Frame 1 (CXorf1, Accession NM\_004709) is another VGAM1828 host target gene. CXorf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXorf1 BINDING SITE, designated SEQ ID:11056, to the nucleotide sequence of VGAM1828 RNA, herein designated VGAM RNA, also designated SEQ ID:4539.

[60760] Another function of VGAM1828 is therefore inhibition of Chromosome X Open Reading Frame 1 (CXorf1, Accession

NM\_004709). Accordingly, utilities of VGAM1828 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXorf1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1829 (VGAM1829) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60761] VGAM1829 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1829 was detected is described hereinabove with reference to Figs. 1-8.

[60762] VGAM1829 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM1829 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60763] VGAM1829 gene encodes a VGAM1829 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1829 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1829 precursor RNA is designated SEQ ID:1815, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1815 is located at position 140030 relative to the genome of Rabbit Fibroma Virus.

[60764] VGAM1829 precursor RNA folds onto itself, forming VGAM1829 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60765] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1829 folded precursor RNA into VGAM1829 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1829 RNA is designated SEQ ID:4540, and

is provided hereinbelow with reference to the sequence listing part.

[60766] VGAM1829 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1829 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1829 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[60767] VGAM1829 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1829 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1829 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1829 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1829 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60768] The complementary binding of VGAM1829 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1829 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1829 host target RNA into VGAM1829 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60769] It is appreciated that VGAM1829 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1829 host target genes. The mRNA of each one of this plurality of VGAM1829 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1829 RNA, herein designated VGAM RNA, and which when bound by VGAM1829 RNA causes inhibition of translation of respective one or more VGAM1829 host target proteins.

[60770] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1829 gene, herein designated VGAM GENE, on one or more VGAM1829 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60771] It is yet further appreciated that a function of VGAM1829 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1829 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM1829 correlate with, and may be deduced from, the identity of the host target genes which VGAM1829 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60772] Nucleotide sequences of the VGAM1829 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1829 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1829 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1829 are further described hereinbelow with reference to Table 1.

[60773] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1829 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1829 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60774] As mentioned hereinabove with reference to Fig. 1, a



function of VGAM1829 gene, herein designated VGAM is inhibition of expression of VGAM1829 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1829 correlate with, and may be deduced from, the identity of the target genes which VGAM1829 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60775] DKFZP564L0864 (Accession XM\_051905) is a VGAM1829 host target gene. DKFZP564L0864 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564L0864, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564L0864 BINDING SITE, designated SEQ ID:35918, to the nucleotide sequence of VGAM1829 RNA, herein designated VGAM RNA, also designated SEQ ID:4540.

[60776] A function of VGAM1829 is therefore inhibition of DKFZP564L0864 (Accession XM\_051905). Accordingly, utilities of VGAM1829 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564L0864. KIAA1596 (Accession XM\_048128) is another VGAM1829 host target gene. KIAA1596 BIND-

ING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1596 BINDING SITE, designated SEQ ID:35119, to the nucleotide sequence of VGAM1829 RNA, herein designated VGAM RNA, also designated SEQ ID:4540.

[60777] Another function of VGAM1829 is therefore inhibition of KIAA1596 (Accession XM\_048128). Accordingly, utilities of VGAM1829 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1596. LOC90246 (Accession XM\_030283) is another VGAM1829 host target gene. LOC90246 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90246, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90246 BINDING SITE, designated SEQ ID:31002, to the nucleotide sequence of VGAM1829 RNA, herein designated VGAM RNA, also designated SEQ ID:4540.

[60778] Another function of VGAM1829 is therefore inhibition of

LOC90246 (Accession XM\_030283). Accordingly, utilities of VGAM1829 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90246. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1830 (VGAM1830) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60779] VGAM1830 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1830 was detected is described hereinabove with reference to Figs. 1-8.

[60780] VGAM1830 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1830 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60781] VGAM1830 gene encodes a VGAM1830 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1830 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1830 precursor RNA is designated SEQ ID:1816, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1816 is located at position 40729 relative to the genome of Camelpox Virus.

[60782] VGAM1830 precursor RNA folds onto itself, forming VGAM1830 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60783] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1830 folded precursor RNA into VGAM1830 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide se-

quence of VGAM1830 RNA is designated SEQ ID:4541, and is provided hereinbelow with reference to the sequence listing part.

[60784] VGAM1830 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1830 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1830 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60785] VGAM1830 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1830 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1830 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1830 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1830 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60786] The complementary binding of VGAM1830 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1830 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1830 host target RNA into VGAM1830 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60787] It is appreciated that VGAM1830 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1830 host target genes. The mRNA of each one of this plurality of VGAM1830 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1830 RNA, herein designated VGAM RNA, and which when bound by VGAM1830 RNA causes inhibition of translation of respective one or more VGAM1830 host target proteins.

[60788] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1830 gene, herein designated VGAM GENE, on one or more VGAM1830 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60789] It is yet further appreciated that a function of VGAM1830

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1830 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1830 correlate with, and may be deduced from, the identity of the host target genes which VGAM1830 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60790] Nucleotide sequences of the VGAM1830 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1830 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1830 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1830 are further described hereinbelow with reference to Table 1.

[60791] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1830 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1830 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.



[60792] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1830 gene, herein designated VGAM is inhibition of expression of VGAM1830 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1830 correlate with, and may be deduced from, the identity of the target genes which VGAM1830 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60793] FLJ12270 (Accession NM\_030581) is a VGAM1830 host target gene. FLJ12270 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12270, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12270 BINDING SITE, designated SEQ ID:24953, to the nucleotide sequence of VGAM1830 RNA, herein designated VGAM RNA, also designated SEQ ID:4541.

[60794] A function of VGAM1830 is therefore inhibition of FLJ12270 (Accession NM\_030581). Accordingly, utilities of VGAM1830 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12270. OSRF (Accession XM\_003724) is another

VGAM1830 host target gene. OSRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSRF BINDING SITE, designated SEQ ID:29941, to the nucleotide sequence of VGAM1830 RNA, herein designated VGAM RNA, also designated SEQ ID:4541.

[60795] Another function of VGAM1830 is therefore inhibition of OSRF (Accession XM\_003724). Accordingly, utilities of VGAM1830 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSRF. POPX1 (Accession NM\_014906) is another VGAM1830 host target gene. POPX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POPX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POPX1 BINDING SITE, designated SEQ ID:17116, to the nucleotide sequence of VGAM1830 RNA, herein designated VGAM RNA, also designated SEQ ID:4541.

[60796] Another function of VGAM1830 is therefore inhibition of POPX1 (Accession NM\_014906). Accordingly, utilities of VGAM1830 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POPX1. LOC124045 (Accession XM\_071873) is another VGAM1830 host target gene. LOC124045 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC124045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124045 BINDING SITE, designated SEQ ID:37439, to the nucleotide sequence of VGAM1830 RNA, herein designated VGAM RNA, also designated SEQ ID:4541.

[60797] Another function of VGAM1830 is therefore inhibition of LOC124045 (Accession XM\_071873). Accordingly, utilities of VGAM1830 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124045. LOC51279 (Accession NM\_016546) is another VGAM1830 host target gene. LOC51279 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51279, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51279 BINDING SITE, designated SEQ ID:18614, to the nucleotide sequence of VGAM1830 RNA, herein designated VGAM RNA, also designated SEQ ID:4541.

[60798] Another function of VGAM1830 is therefore inhibition of LOC51279 (Accession NM\_016546). Accordingly, utilities of VGAM1830 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51279. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1831 (VGAM1831) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60799] VGAM1831 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1831 was detected is described hereinabove with reference to Figs. 1–8.

[60800] VGAM1831 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1831 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[60801] VGAM1831 gene encodes a VGAM1831 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1831 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1831 precursor RNA is designated SEQ ID:1817, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1817 is located at position 40965 relative to the genome of Camelpox Virus.

[60802] VGAM1831 precursor RNA folds onto itself, forming VGAM1831 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60803] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1831 folded precursor RNA into VGAM1831

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM1831 RNA is designated SEQ ID:4542, and is provided hereinbelow with reference to the sequence listing part.

[60804] VGAM1831 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1831 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1831 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60805] VGAM1831 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1831 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1831 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1831 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1831 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60806] The complementary binding of VGAM1831 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1831 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1831 host target RNA into VGAM1831 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[60807] It is appreciated that VGAM1831 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1831 host target genes. The mRNA of each one of this plurality of VGAM1831 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1831 RNA, herein designated VGAM RNA, and which when bound by VGAM1831 RNA causes inhibition of translation of respective one or more VGAM1831 host target proteins.

[60808] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1831 gene, herein designated VGAM GENE, on one or more VGAM1831 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60809] It is yet further appreciated that a function of VGAM1831 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1831 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1831 correlate with, and may be deduced from, the identity of the host target genes which VGAM1831 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60810] Nucleotide sequences of the VGAM1831 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1831 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1831 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1831 are further described hereinbelow with reference to Table 1.

[60811] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1831 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1831 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60812] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1831 gene, herein designated VGAM is inhibition of expression of VGAM1831 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1831 correlate with, and may be deduced from, the identity of the target genes which VGAM1831 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60813] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM\_004776) is a VGAM1831 host target gene. B4GALT5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT5 BINDING SITE, designated SEQ ID:11170, to the nucleotide

sequence of VGAM1831 RNA, herein designated VGAM RNA, also designated SEQ ID:4542.

[60814] A function of VGAM1831 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM\_004776). Accordingly, utilities of VGAM1831 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT5. BCL2-antagonist/killer 1 (BAK1, Accession XM\_166333) is another VGAM1831 host target gene. BAK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BAK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAK1 BINDING SITE, designated SEQ ID:44175, to the nucleotide sequence of VGAM1831 RNA, herein designated VGAM RNA, also designated SEQ ID:4542.

[60815] Another function of VGAM1831 is therefore inhibition of BCL2-antagonist/killer 1 (BAK1, Accession XM\_166333), a gene which accelerates programmed cell death by binding to, and antagonizing the a repressor bcl-2. Accordingly, utilities of VGAM1831 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with BAK1. The function of BAK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430.Forkhead Box O1A

(rhabdomyosarcoma) (FOXO1A, Accession NM\_002015) is another VGAM1831 host target gene. FOXO1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXO1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXO1A BINDING SITE, designated SEQ ID:7758, to the nucleotide sequence of VGAM1831 RNA, herein designated VGAM RNA, also designated SEQ ID:4542.

[60816] Another function of VGAM1831 is therefore inhibition of Forkhead Box O1A (rhabdomyosarcoma) (FOXO1A, Accession NM\_002015), a gene which is a probable transcription factor. Accordingly, utilities of VGAM1831 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXO1A. The function of FOXO1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM228.Angiomotin Like 2 (AMOTL2, Accession NM\_016201) is another VGAM1831 host target gene. AMOTL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AMOTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOTL2 BINDING SITE, designated SEQ ID:18293, to the nucleotide sequence of VGAM1831 RNA, herein designated VGAM RNA, also designated SEQ ID:4542.

[60817] Another function of VGAM1831 is therefore inhibition of Angiomotin Like 2 (AMOTL2, Accession NM\_016201). Accordingly, utilities of VGAM1831 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOTL2. FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM\_054016) is another VGAM1831 host target gene. FUSIP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FUSIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUSIP1 BIND-

ING SITE, designated SEQ ID:27624, to the nucleotide sequence of VGAM1831 RNA, herein designated VGAM RNA, also designated SEQ ID:4542.

[60818] Another function of VGAM1831 is therefore inhibition of FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM\_054016). Accordingly, utilities of VGAM1831 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUSIP1. MGC10999 (Accession NM\_032307) is another VGAM1831 host target gene. MGC10999 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10999, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10999 BINDING SITE, designated SEQ ID:26090, to the nucleotide sequence of VGAM1831 RNA, herein designated VGAM RNA, also designated SEQ ID:4542.

[60819] Another function of VGAM1831 is therefore inhibition of MGC10999 (Accession NM\_032307). Accordingly, utilities of VGAM1831 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10999. LOC153259 (Accession XM\_098342) is an-

other VGAM1831 host target gene. LOC153259 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153259, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153259 BINDING SITE, designated SEQ ID:41600, to the nucleotide sequence of VGAM1831 RNA, herein designated VGAM RNA, also designated SEQ ID:4542.

[60820] Another function of VGAM1831 is therefore inhibition of LOC153259 (Accession XM\_098342). Accordingly, utilities of VGAM1831 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153259. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1832 (VGAM1832) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60821] VGAM1832 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1832 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[60822] VGAM1832 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus.

VGAM1832 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60823] VGAM1832 gene encodes a VGAM1832 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1832 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1832 precursor RNA is designated SEQ ID:1818, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1818 is located at position 38937 relative to the genome of Camelpox Virus.

[60824] VGAM1832 precursor RNA folds onto itself, forming VGAM1832 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA



gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60825] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1832 folded precursor RNA into VGAM1832 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1832 RNA is designated SEQ ID:4543, and is provided hereinbelow with reference to the sequence listing part.

[60826] VGAM1832 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1832 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1832 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60827] VGAM1832 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1832 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1832 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1832 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1832 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60828] The complementary binding of VGAM1832 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1832 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1832 host target RNA into VGAM1832 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60829] It is appreciated that VGAM1832 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1832 host target genes. The mRNA of each one of this plurality of VGAM1832 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1832 RNA, herein designated VGAM RNA, and which when bound by VGAM1832 RNA causes inhibition of translation of respective one or more VGAM1832 host target proteins.

[60830] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1832 gene, herein designated VGAM GENE, on one or more VGAM1832 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60831] It is yet further appreciated that a function of VGAM1832 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1832 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1832 correlate with, and may be deduced from, the identity of the host target genes which VGAM1832 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60832] Nucleotide sequences of the VGAM1832 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1832 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1832 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1832 are further described hereinbelow with reference to Table 1.

[60833] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1832 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1832 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60834] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1832 gene, herein designated VGAM is inhibition of expression of VGAM1832 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1832 correlate with, and may be deduced from, the identity of the target genes which VGAM1832 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60835] GA (Accession NM\_013267) is a VGAM1832 host target gene. GA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of GA BINDING SITE, designated SEQ ID:14936, to the nucleotide sequence of VGAM1832 RNA, herein designated VGAM RNA, also designated SEQ ID:4543.

[60836] A function of VGAM1832 is therefore inhibition of GA (Accession NM\_013267). Accordingly, utilities of VGAM1832 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GA. KIAA0753 (Accession NM\_014804) is another VGAM1832 host target gene. KIAA0753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0753 BINDING SITE, designated SEQ ID:16737, to the nucleotide sequence of VGAM1832 RNA, herein designated VGAM RNA, also designated SEQ ID:4543.

[60837] Another function of VGAM1832 is therefore inhibition of KIAA0753 (Accession NM\_014804). Accordingly, utilities of VGAM1832 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0753. KIAA1130 (Accession XM\_031104) is another

VGAM1832 host target gene. KIAA1130 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1130 BINDING SITE, designated SEQ ID:31289, to the nucleotide sequence of VGAM1832 RNA, herein designated VGAM RNA, also designated SEQ ID:4543.

[60838] Another function of VGAM1832 is therefore inhibition of KIAA1130 (Accession XM\_031104). Accordingly, utilities of VGAM1832 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1130. Ribosomal Protein L36 (RPL36, Accession NM\_015414) is another VGAM1832 host target gene. RPL36 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RPL36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPL36 BINDING SITE, designated SEQ ID:17715, to the nucleotide sequence of VGAM1832 RNA, herein designated VGAM RNA, also designated SEQ

ID:4543.

[60839] Another function of VGAM1832 is therefore inhibition of Ribosomal Protein L36 (RPL36, Accession NM\_015414). Accordingly, utilities of VGAM1832 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPL36. LOC56920 (Accession NM\_020163) is another VGAM1832 host target gene. LOC56920 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC56920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56920 BINDING SITE, designated SEQ ID:21381, to the nucleotide sequence of VGAM1832 RNA, herein designated VGAM RNA, also designated SEQ ID:4543.

[60840] Another function of VGAM1832 is therefore inhibition of LOC56920 (Accession NM\_020163). Accordingly, utilities of VGAM1832 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56920. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-



dress Messenger 1833 (VGAM1833) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60841] VGAM1833 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1833 was detected is described hereinabove with reference to Figs. 1–8.

[60842] VGAM1833 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1833 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60843] VGAM1833 gene encodes a VGAM1833 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1833 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1833 precursor RNA is designated SEQ ID:1819, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1819 is located at position 38839 relative to the genome of Camelpox Virus.

[60844] VGAM1833 precursor RNA folds onto itself, forming VGAM1833 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60845] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1833 folded precursor RNA into VGAM1833 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1833 RNA is designated SEQ ID:4544, and is provided hereinbelow with reference to the sequence listing part.

[60846] VGAM1833 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1833 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1833 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60847] VGAM1833 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1833 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1833 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1833 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1833 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[60848] The complementary binding of VGAM1833 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1833 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1833 host target RNA into VGAM1833 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60849] It is appreciated that VGAM1833 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1833 host target genes. The mRNA of each one of this plurality of VGAM1833 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1833 RNA, herein designated VGAM RNA, and which when bound by VGAM1833 RNA causes inhibition of translation of respective one or more VGAM1833 host target proteins.

[60850] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1833 gene, herein designated VGAM GENE, on one or more VGAM1833 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60851] It is yet further appreciated that a function of VGAM1833 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1833 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1833 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60852] Nucleotide sequences of the VGAM1833 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1833 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1833 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1833 are further described hereinbelow with reference to Table 1.

[60853] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1833 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1833 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60854] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1833 gene, herein designated VGAM is inhibition of expression of VGAM1833 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1833 correlate with, and may be deduced from, the identity of the target genes which VGAM1833

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60855] Carbonic Anhydrase XII (CA12, Accession NM\_001218) is a VGAM1833 host target gene. CA12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CA12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CA12 BINDING SITE, designated SEQ ID:6881, to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60856] A function of VGAM1833 is therefore inhibition of Carbonic Anhydrase XII (CA12, Accession NM\_001218), a gene which functions in cellular transport and metabolic processes. Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CA12. The function of CA12 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM508. Cytoplasmic Linker Associated Protein 2 (CLASP2, Accession XM\_035453) is another VGAM1833

host target gene. CLASP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLASP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLASP2 BINDING SITE, designated SEQ ID:32270, to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60857] Another function of VGAM1833 is therefore inhibition of Cytoplasmic Linker Associated Protein 2 (CLASP2, Accession XM\_035453), a gene which is involved in the regional regulation of microtubule dynamics in motile fibroblasts. Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLASP2. The function of CLASP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM897.G Protein-coupled Receptor 48 (GPR48, Accession NM\_018490) is another VGAM1833 host target gene. GPR48 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GPR48, corre-



sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR48 BINDING SITE, designated SEQ ID:20549, to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60858] Another function of VGAM1833 is therefore inhibition of G Protein-coupled Receptor 48 (GPR48, Accession NM\_018490), a gene which binds to follicle-stimulating hormone and thyroid-stimulating hormone. Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR48. The function of GPR48 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM376. Ladinin 1 (LAD1, Accession NM\_005558) is another VGAM1833 host target gene. LAD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAD1 BINDING SITE, designated SEQ ID:12083,

to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60859] Another function of VGAM1833 is therefore inhibition of Ladinin 1 (LAD1, Accession NM\_005558). Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAD1. Phosphatidylinositol Glycan, Class A (paroxysmal nocturnal hemoglobinuria) (PIGA, Accession NM\_020472) is another VGAM1833 host target gene. PIGA BINDING SITE1 and PIGA BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PIGA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIGA BINDING SITE1 and PIGA BINDING SITE2, designated SEQ ID:21710 and SEQ ID:21717 respectively, to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60860] Another function of VGAM1833 is therefore inhibition of Phosphatidylinositol Glycan, Class A (paroxysmal nocturnal hemoglobinuria) (PIGA, Accession NM\_020472). Accordingly, utilities of VGAM1833 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with PIGA. Exportin 1 (CRM1 homolog, yeast) (XPO1, Accession NM\_003400) is another VGAM1833 host target gene. XPO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XPO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XPO1 BINDING SITE, designated SEQ ID:9436, to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60861] Another function of VGAM1833 is therefore inhibition of Exportin 1 (CRM1 homolog, yeast) (XPO1, Accession NM\_003400), a gene which is the cell cycle-regulated nuclear export protein 1. Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XPO1. The function of XPO1 has been established by previous studies. Human CRM1, or XPO1, is the homolog of yeast crm1 (named for 'required for chromosome region maintenance'), a nuclear protein essential for proliferation and chromosome region maintenance. Fornerod et al. (1997) used the oncogenic

nucleoporin CAN (OMIM Ref. No. 114350) to coprecipitate human CRM1. The complete cDNA encodes a predicted protein of 1,071 amino acids with a predicted molecular mass of 123 kD. The CRM1 protein migrates at 112 kD. Human CRM1 has 47% identity with *S. cerevisiae* crm1 and 52% identity with *S. pombe* crm1+. The N terminus of human CRM1 shares significant homology with the N terminus of importin-beta. Fornerod et al. (1997) identified a group of largely uncharacterized yeast and vertebrate proteins of similar size (110 to 120 kD) that share this homology domain, which they proposed to call the CRIME domain (for 'CRM1, importin-beta, etc.'). Kudo et al. (1997) cloned human CRM1 cDNA using sequence information from EST databases and a PCR-based strategy based on the sequence of *S. pombe* crm1+. Northern blot analysis using the C-terminal region of human CRM1 cDNA as a probe revealed a major transcript of 5.6 kb expressed in all tissues tested except kidney. Human CRM1 weakly complemented the cold-sensitive mutation of *S. pombe* crm1-809. Overproduction of human CRM1 suppressed cell proliferation in wildtype *S. pombe* in an expression level-dependent manner. Overexpression of native *S. pombe* crm1+ had the same effect. Northern blot

analysis with RNAs isolated from synchronized mammalian cells showed that the expression of mammalian CRM1 was initiated in the late G1 phase and reached a peak at G2/M, although the protein level did not change during the cell cycle. Human CRM1 fused to green fluorescent protein (GFP) and transiently expressed in NIH 3T3 cells showed that human CRM1 was localized preferentially in the nuclear envelope, but was also detectable in the nucleoplasm and the cytoplasm. A *crm1* mutation of *S. pombe* caused nuclear import of a GFP fusion protein containing a nuclear export signal (NES) but no change in the distribution of a GFP fusion protein containing a nuclear localization signal (NLS). These data suggested to Kudo et al. (1997) that CRM1 is a novel cell cycle-regulated gene that is essential for the NES-dependent nuclear export of proteins.

[60862] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[60863] Fornerod, M.; van Duersen, J.; van Baal, S.; Reynolds, A.; Davis, D.; Murti, K. G.; Fransen, J.; Grosveld, G. : The human homologue of yeast CRM1 is in a dynamic subcomplex with CAN/Nup214 and a novel nuclear pore compo-

nent Nup88. EMBO J. 16: 807–816, 1997. ; and

[60864] Kudo, N.; Khochbin, S.; Nishi, K.; Kitano, K.; Yanagida, M.; Yoshida, M.; Horinouchi, S. : Molecular cloning and cell cycle–dependent expression of mammalian CRM1, a protein involved in.

[60865] Further studies establishing the function and utilities of XPO1 are found in John Hopkins OMIM database record ID 602559, and in cited publications numbered 5912, 12100–633 and 9267 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0368 (Accession XM\_036708) is another VGAM1833 host target gene. KIAA0368 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0368, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0368 BINDING SITE, designated SEQ ID:32487, to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60866] Another function of VGAM1833 is therefore inhibition of KIAA0368 (Accession XM\_036708). Accordingly, utilities of VGAM1833 include diagnosis, prevention and treat–

ment of diseases and clinical conditions associated with KIAA0368. KIAA1018 (Accession NM\_014967) is another VGAM1833 host target gene. KIAA1018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1018 BINDING SITE, designated SEQ ID:17358, to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60867] Another function of VGAM1833 is therefore inhibition of KIAA1018 (Accession NM\_014967). Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1018. KIAA1576 (Accession XM\_038186) is another VGAM1833 host target gene. KIAA1576 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1576 BINDING SITE, designated SEQ ID:32769, to the

nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60868] Another function of VGAM1833 is therefore inhibition of KIAA1576 (Accession XM\_038186). Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1576. Translocase of Outer Mitochondrial Membrane 70 Homolog A (yeast) (TOMM70A, Accession NM\_014820) is another VGAM1833 host target gene. TOMM70A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOMM70A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOMM70A BINDING SITE, designated SEQ ID:16791, to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60869] Another function of VGAM1833 is therefore inhibition of Translocase of Outer Mitochondrial Membrane 70 Homolog A (yeast) (TOMM70A, Accession NM\_014820). Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOMM70A. LOC158527 (Accession



XM\_088594) is another VGAM1833 host target gene.

LOC158527 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158527 BINDING SITE, designated SEQ ID:39862, to the nucleotide sequence of VGAM1833 RNA, herein designated VGAM RNA, also designated SEQ ID:4544.

[60870] Another function of VGAM1833 is therefore inhibition of LOC158527 (Accession XM\_088594). Accordingly, utilities of VGAM1833 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158527. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1834 (VGAM1834) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60871] VGAM1834 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1834 was detected is described hereinabove with reference to Figs. 1–8.

[60872] VGAM1834 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus.

VGAM1834 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60873] VGAM1834 gene encodes a VGAM1834 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1834 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1834 precursor RNA is designated SEQ ID:1820, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1820 is located at position 36702 relative to the genome of Camelpox Virus.

[60874] VGAM1834 precursor RNA folds onto itself, forming VGAM1834 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60875] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1834 folded precursor RNA into VGAM1834 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1834 RNA is designated SEQ ID:4545, and is provided hereinbelow with reference to the sequence listing part.

[60876] VGAM1834 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1834 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1834 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60877] VGAM1834 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1834 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1834 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1834 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1834 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[60878] The complementary binding of VGAM1834 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1834 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1834 host target RNA into VGAM1834 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60879] It is appreciated that VGAM1834 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1834 host target genes. The mRNA of each one of this plurality of VGAM1834 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1834 RNA, herein designated VGAM RNA, and which when bound by VGAM1834 RNA causes inhibition of translation of respective one or more VGAM1834 host target proteins.

[60880] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1834 gene, herein designated VGAM GENE, on one or more VGAM1834 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60881] It is yet further appreciated that a function of VGAM1834 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1834 correlate with, and may be deduced from, the identity of the host target genes which VGAM1834 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60882] Nucleotide sequences of the VGAM1834 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1834 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1834 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1834 are further described hereinbelow with reference to Table 1.

[60883] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1834 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1834 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60884] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1834 gene, herein designated VGAM is inhibition of expression of VGAM1834 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1834 correlate with, and may be deduced from, the identity of the target genes which VGAM1834 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60885] E2F Transcription Factor 3 (E2F3, Accession NM\_001949) is a VGAM1834 host target gene. E2F3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by E2F3, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of E2F3 BINDING SITE, designated SEQ ID:7670, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60886] A function of VGAM1834 is therefore inhibition of E2F Transcription Factor 3 (E2F3, Accession NM\_001949), a gene which binds dna and controls cell-cycle progression from g1 to s phase. Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E2F3. The function of E2F3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM475.Homeo Box B3 (HOXB3, Accession NM\_002146) is another VGAM1834 host target gene. HOXB3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HOXB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXB3 BINDING SITE, designated SEQ ID:7924, to the nu-



cleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60887] Another function of VGAM1834 is therefore inhibition of Homeo Box B3 (HOXB3, Accession NM\_002146). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXB3. Nuclear Receptor Subfamily 1, Group I, Member 2 (NR1I2, Accession NM\_003889) is another VGAM1834 host target gene. NR1I2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NR1I2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR1I2 BINDING SITE, designated SEQ ID:9975, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60888] Another function of VGAM1834 is therefore inhibition of Nuclear Receptor Subfamily 1, Group I, Member 2 (NR1I2, Accession NM\_003889), a gene which binds to a response element in the cyp3a4 gene promoter and activates its expression in response to a wide variety of endobiotics and xenobiotics. Accordingly, utilities of VGAM1834 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with NR1I2. The function of NR1I2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM336. Neural Retina Leucine Zipper (NRL, Accession NM\_006177) is another VGAM1834 host target gene. NRL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRL BINDING SITE, designated SEQ ID:12840, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60889] Another function of VGAM1834 is therefore inhibition of Neural Retina Leucine Zipper (NRL, Accession NM\_006177), a gene which has a basic motif and a leucine zipper domain similar to jun and fos. Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRL. The function of NRL and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM419. Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM\_138694) is another VGAM1834 host target gene. PKHD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKHD1 BINDING SITE, designated SEQ ID:28947, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60890] Another function of VGAM1834 is therefore inhibition of Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM\_138694). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKHD1. Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM\_003038) is another VGAM1834 host target gene. SLC1A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A4, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A4 BINDING SITE, designated SEQ ID:9000, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60891] Another function of VGAM1834 is therefore inhibition of Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM\_003038), a gene which transports alanine, serine, cysteine, and threonine. exhibits sodium dependence. Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A4. The function of SLC1A4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM859.BCMP1 (Accession NM\_031442) is another VGAM1834 host target gene. BCMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of BCMP1 BINDING SITE, designated SEQ ID:25460, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60892] Another function of VGAM1834 is therefore inhibition of BCMP1 (Accession NM\_031442). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCMP1. DIM1 (Accession NM\_006701) is another VGAM1834 host target gene. DIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIM1 BINDING SITE, designated SEQ ID:13525, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60893] Another function of VGAM1834 is therefore inhibition of DIM1 (Accession NM\_006701). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIM1. FLJ10738 (Accession NM\_018199) is another VGAM1834

host target gene. FLJ10738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10738 BINDING SITE, designated SEQ ID:20071, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60894] Another function of VGAM1834 is therefore inhibition of FLJ10738 (Accession NM\_018199). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10738. KIAA0040 (Accession NM\_014656) is another VGAM1834 host target gene. KIAA0040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0040 BINDING SITE, designated SEQ ID:16101, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60895] Another function of VGAM1834 is therefore inhibition of KIAA0040 (Accession NM\_014656). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0040. KIAA0261 (Accession XM\_042946) is another VGAM1834 host target gene. KIAA0261 BINDING SITE1 and KIAA0261 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0261, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0261 BINDING SITE1 and KIAA0261 BINDING SITE2, designated SEQ ID:33831 and SEQ ID:33837 respectively, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60896] Another function of VGAM1834 is therefore inhibition of KIAA0261 (Accession XM\_042946). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0261. LOC149842 (Accession XM\_097745) is another VGAM1834 host target gene. LOC149842 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC149842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149842 BINDING SITE, designated SEQ ID:41093, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60897] Another function of VGAM1834 is therefore inhibition of LOC149842 (Accession XM\_097745). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149842. LOC150967 (Accession XM\_087060) is another VGAM1834 host target gene. LOC150967 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150967, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150967 BINDING SITE, designated SEQ ID:39038, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60898] Another function of VGAM1834 is therefore inhibition of LOC150967 (Accession XM\_087060). Accordingly, utilities



of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150967. LOC152503 (Accession XM\_098238) is another VGAM1834 host target gene. LOC152503 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152503, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152503 BINDING SITE, designated SEQ ID:41520, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60899] Another function of VGAM1834 is therefore inhibition of LOC152503 (Accession XM\_098238). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152503. LOC221495 (Accession XM\_168136) is another VGAM1834 host target gene. LOC221495 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC221495 BINDING SITE, designated SEQ ID:45063, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60900] Another function of VGAM1834 is therefore inhibition of LOC221495 (Accession XM\_168136). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221495. LOC221935 (Accession XM\_166537) is another VGAM1834 host target gene. LOC221935 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221935 BINDING SITE, designated SEQ ID:44504, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60901] Another function of VGAM1834 is therefore inhibition of LOC221935 (Accession XM\_166537). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221935. LOC254100 (Accession XM\_172851) is another VGAM1834 host target gene. LOC254100 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254100 BINDING SITE, designated SEQ ID:46129, to the nucleotide sequence of VGAM1834 RNA, herein designated VGAM RNA, also designated SEQ ID:4545.

[60902] Another function of VGAM1834 is therefore inhibition of LOC254100 (Accession XM\_172851). Accordingly, utilities of VGAM1834 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254100. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1835 (VGAM1835) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60903] VGAM1835 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1835 was detected is described hereinabove with reference to Figs. 1-8.

[60904] VGAM1835 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1835 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60905] VGAM1835 gene encodes a VGAM1835 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1835 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1835 precursor RNA is designated SEQ ID:1821, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1821 is located at position 136546 relative to the genome of Fowlpox Virus.

[60906] VGAM1835 precursor RNA folds onto itself, forming VGAM1835 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[60907] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1835 folded precursor RNA into VGAM1835 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1835 RNA is designated SEQ ID:4546, and is provided hereinbelow with reference to the sequence listing part.

[60908] VGAM1835 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1835 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1835 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60909] VGAM1835 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1835 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1835 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1835 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1835 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[60910] The complementary binding of VGAM1835 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1835 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1835 host target RNA into VGAM1835 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60911] It is appreciated that VGAM1835 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1835 host target genes. The mRNA of each one of this plurality of VGAM1835 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1835 RNA, herein designated VGAM RNA, and which when bound by VGAM1835 RNA causes inhibition of translation of respective one or more VGAM1835 host target proteins.

[60912] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1835 gene, herein designated VGAM GENE, on one or more VGAM1835 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60913] It is yet further appreciated that a function of VGAM1835 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1835 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1835 correlate with, and may be deduced from, the identity of the host target genes which VGAM1835 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60914] Nucleotide sequences of the VGAM1835 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1835 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1835 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, of VGAM1835 are further described hereinbelow with reference to Table 1.

[60915] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1835 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1835 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60916] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1835 gene, herein designated VGAM is inhibition of expression of VGAM1835 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1835 correlate with, and may be deduced from, the identity of the target genes which VGAM1835 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60917] Dihydropyrimidinase-like 3 (DPYSL3, Accession NM\_001387) is a VGAM1835 host target gene. DPYSL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DPYSL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of DPYSL3 BINDING SITE, designated SEQ ID:7068, to the nucleotide sequence of VGAM1835 RNA, herein designated VGAM RNA, also designated SEQ ID:4546.

[60918] A function of VGAM1835 is therefore inhibition of Dihydropyrimidinase-like 3 (DPYSL3, Accession NM\_001387), a gene which is a member of the dihydropyrimidinase family. Accordingly, utilities of VGAM1835 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYSL3. The function of DPYSL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM24. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1836 (VGAM1836) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60919] VGAM1836 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1836 was detected is described hereinabove with reference to Figs. 1–8.

[60920] VGAM1836 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1836 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60921] VGAM1836 gene encodes a VGAM1836 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1836 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1836 precursor RNA is designated SEQ ID:1822, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1822 is located at position 140071 relative to the genome of Fowlpox Virus.

[60922] VGAM1836 precursor RNA folds onto itself, forming VGAM1836 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[60923] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1836 folded precursor RNA into VGAM1836 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1836 RNA is designated SEQ ID:4547, and is provided hereinbelow with reference to the sequence listing part.

[60924] VGAM1836 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1836 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1836 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60925] VGAM1836 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1836 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1836 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1836 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1836 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60926] The complementary binding of VGAM1836 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1836 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1836 host target RNA into VGAM1836 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60927] It is appreciated that VGAM1836 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1836 host target genes. The mRNA of each one of this plurality of VGAM1836 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1836 RNA, herein designated VGAM RNA, and which when bound by VGAM1836 RNA causes inhibition of translation of respective one or more VGAM1836 host target proteins.

[60928] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1836 gene, herein designated VGAM GENE, on one or more VGAM1836 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60929] It is yet further appreciated that a function of VGAM1836 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1836 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1836 correlate with, and may be deduced from, the identity of the host target genes which VGAM1836 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60930] Nucleotide sequences of the VGAM1836 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1836 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1836 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1836 are further described hereinbelow with reference to Table 1.

[60931] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1836 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1836 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60932] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1836 gene, herein designated VGAM is inhibition of expression of VGAM1836 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1836 correlate with, and may be deduced from, the identity of the target genes which VGAM1836 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60933] KIAA1856 (Accession XM\_166549) is a VGAM1836 host target gene. KIAA1856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity



of the nucleotide sequences of KIAA1856 BINDING SITE, designated SEQ ID:44526, to the nucleotide sequence of VGAM1836 RNA, herein designated VGAM RNA, also designated SEQ ID:4547.

[60934] A function of VGAM1836 is therefore inhibition of KIAA1856 (Accession XM\_166549). Accordingly, utilities of VGAM1836 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1856. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1837 (VGAM1837) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60935] VGAM1837 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1837 was detected is described hereinabove with reference to Figs. 1–8.

[60936] VGAM1837 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1837 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[60937] VGAM1837 gene encodes a VGAM1837 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1837 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1837 precursor RNA is designated SEQ ID:1823, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1823 is located at position 133890 relative to the genome of Fowlpox Virus.

[60938] VGAM1837 precursor RNA folds onto itself, forming VGAM1837 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60939] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1837 folded precursor RNA into VGAM1837 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1837 RNA is designated SEQ ID:4548, and is provided hereinbelow with reference to the sequence listing part.

[60940] VGAM1837 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1837 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1837 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60941] VGAM1837 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1837 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1837 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1837 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1837 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60942] The complementary binding of VGAM1837 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1837 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1837 host target RNA into VGAM1837 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[60943] It is appreciated that VGAM1837 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1837 host target genes. The mRNA of each one of this plurality of VGAM1837 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1837 RNA, herein designated VGAM RNA, and which when bound by VGAM1837 RNA causes inhibition of translation of respective one or more VGAM1837 host target proteins.

[60944] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1837 gene, herein designated VGAM GENE, on one or more VGAM1837 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60945] It is yet further appreciated that a function of VGAM1837 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1837 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1837 correlate with, and may be deduced from, the identity of the host target genes which VGAM1837 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60946] Nucleotide sequences of the VGAM1837 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1837 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1837 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1837 are further described hereinbelow with reference to Table 1.

[60947] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1837 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1837 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60948] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1837 gene, herein designated VGAM is inhibition of expression of VGAM1837 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1837 correlate with, and may be deduced from, the identity of the target genes which VGAM1837 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60949] Contactin Associated Protein-like 2 (CNTNAP2, Accession NM\_014141) is a VGAM1837 host target gene. CNTNAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNTNAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNTNAP2 BINDING SITE, designated SEQ ID:15413, to the nucleotide sequence of VGAM1837 RNA, herein designated VGAM RNA, also designated SEQ

ID:4548.

[60950] A function of VGAM1837 is therefore inhibition of Contactin Associated Protein-like 2 (CNTNAP2, Accession NM\_014141). Accordingly, utilities of VGAM1837 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNTNAP2. G Protein-coupled Receptor 65 (GPR65, Accession XM\_007392) is another VGAM1837 host target gene. GPR65 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GPR65, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR65 BINDING SITE, designated SEQ ID:30051, to the nucleotide sequence of VGAM1837 RNA, herein designated VGAM RNA, also designated SEQ ID:4548.

[60951] Another function of VGAM1837 is therefore inhibition of G Protein-coupled Receptor 65 (GPR65, Accession XM\_007392). Accordingly, utilities of VGAM1837 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR65. Neurexin 1 (NRXN1, Accession NM\_138735) is another VGAM1837 host target gene. NRXN1 BINDING SITE1 and NRXN1 BINDING SITE2



are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NRXN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRXN1 BINDING SITE1 and NRXN1 BINDING SITE2, designated SEQ ID:28992 and SEQ ID:11221 respectively, to the nucleotide sequence of VGAM1837 RNA, herein designated VGAM RNA, also designated SEQ ID:4548.

[60952] Another function of VGAM1837 is therefore inhibition of Neurexin 1 (NRXN1, Accession NM\_138735), a gene which may be involved in cell recognition, cell adhesion, and mediate intracellular signaling. Accordingly, utilities of VGAM1837 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRXN1. The function of NRXN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Ectonucleotide Pyrophosphatase/phosphodiesterase 4 (putative function) (ENPP4, Accession NM\_014936) is another VGAM1837 host target gene. ENPP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENPP4,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENPP4 BINDING SITE, designated SEQ ID:17239, to the nucleotide sequence of VGAM1837 RNA, herein designated VGAM RNA, also designated SEQ ID:4548.

[60953] Another function of VGAM1837 is therefore inhibition of Ectonucleotide Pyrophosphatase/phosphodiesterase 4 (putative function) (ENPP4, Accession NM\_014936). Accordingly, utilities of VGAM1837 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENPP4. LOC148824 (Accession XM\_097527) is another VGAM1837 host target gene. LOC148824 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148824 BINDING SITE, designated SEQ ID:40909, to the nucleotide sequence of VGAM1837 RNA, herein designated VGAM RNA, also designated SEQ ID:4548.

[60954] Another function of VGAM1837 is therefore inhibition of LOC148824 (Accession XM\_097527). Accordingly, utilities of VGAM1837 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148824. LOC153711 (Accession XM\_098419) is another VGAM1837 host target gene. LOC153711 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153711 BINDING SITE, designated SEQ ID:41665, to the nucleotide sequence of VGAM1837 RNA, herein designated VGAM RNA, also designated SEQ ID:4548.

[60955] Another function of VGAM1837 is therefore inhibition of LOC153711 (Accession XM\_098419). Accordingly, utilities of VGAM1837 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153711. LOC253664 (Accession XM\_170673) is another VGAM1837 host target gene. LOC253664 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253664, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253664 BINDING SITE, designated SEQ ID:45446, to the nucleotide sequence of VGAM1837 RNA, herein designated VGAM RNA, also designated SEQ ID:4548.

[60956] Another function of VGAM1837 is therefore inhibition of LOC253664 (Accession XM\_170673). Accordingly, utilities of VGAM1837 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253664. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1838 (VGAM1838) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60957] VGAM1838 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1838 was detected is described hereinabove with reference to Figs. 1-8.

[60958] VGAM1838 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1838 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[60959] VGAM1838 gene encodes a VGAM1838 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1838 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1838 precursor RNA is designated SEQ ID:1824, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1824 is located at position 131052 relative to the genome of Fowlpox Virus.

[60960] VGAM1838 precursor RNA folds onto itself, forming VGAM1838 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60961] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1838 folded precursor RNA into VGAM1838

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1838 RNA is designated SEQ ID:4549, and is provided hereinbelow with reference to the sequence listing part.

[60962] VGAM1838 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1838 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1838 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60963] VGAM1838 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1838 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1838 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1838 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1838 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60964] The complementary binding of VGAM1838 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1838 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1838 host target RNA into VGAM1838 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[60965] It is appreciated that VGAM1838 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1838 host target genes. The mRNA of each one of this plurality of VGAM1838 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1838 RNA, herein designated VGAM RNA, and which when bound by VGAM1838 RNA causes inhibition of translation of respective one or more VGAM1838 host target proteins.

[60966] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1838 gene, herein designated VGAM GENE, on one or more VGAM1838 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60967] It is yet further appreciated that a function of VGAM1838 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1838 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1838 correlate with, and may be deduced from, the identity of the host target genes which VGAM1838 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60968] Nucleotide sequences of the VGAM1838 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1838 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1838 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1838 are further described hereinbelow with reference to Table 1.

[60969] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1838 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1838 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60970] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1838 gene, herein designated VGAM is inhibition of expression of VGAM1838 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1838 correlate with, and may be deduced from, the identity of the target genes which VGAM1838 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60971] Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III) (AGL, Accession NM\_000028) is a VGAM1838 host target gene. AGL BINDING SITE1 through AGL BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AGL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGL BINDING

SITE1 through AGL BINDING SITE6, designated SEQ ID:5466, SEQ ID:6305, SEQ ID:6298, SEQ ID:6293, SEQ ID:6288 and SEQ ID:6283 respectively, to the nucleotide sequence of VGAM1838 RNA, herein designated VGAM RNA, also designated SEQ ID:4549.

[60972] A function of VGAM1838 is therefore inhibition of Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III) (AGL, Accession NM\_000028). Accordingly, utilities of VGAM1838 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGL. Syntrophin, Gamma 1 (SNTG1, Accession NM\_018967) is another VGAM1838 host target gene. SNTG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNTG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNTG1 BINDING SITE, designated SEQ ID:21039, to the nucleotide sequence of VGAM1838 RNA, herein designated VGAM RNA, also designated SEQ ID:4549.

[60973] Another function of VGAM1838 is therefore inhibition of Syntrophin, Gamma 1 (SNTG1, Accession NM\_018967).

Accordingly, utilities of VGAM1838 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNTG1. LOC133686 (Accession XM\_059667) is another VGAM1838 host target gene. LOC133686 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC133686, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133686 BINDING SITE, designated SEQ ID:37052, to the nucleotide sequence of VGAM1838 RNA, herein designated VGAM RNA, also designated SEQ ID:4549.

[60974] Another function of VGAM1838 is therefore inhibition of LOC133686 (Accession XM\_059667). Accordingly, utilities of VGAM1838 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133686. LOC91301 (Accession XM\_037564) is another VGAM1838 host target gene. LOC91301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC91301 BINDING SITE, designated SEQ ID:32649, to the nucleotide sequence of VGAM1838 RNA, herein designated VGAM RNA, also designated SEQ ID:4549.

[60975] Another function of VGAM1838 is therefore inhibition of LOC91301 (Accession XM\_037564). Accordingly, utilities of VGAM1838 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91301. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1839 (VGAM1839) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60976] VGAM1839 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1839 was detected is described hereinabove with reference to Figs. 1–8.

[60977] VGAM1839 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1839 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[60978] VGAM1839 gene encodes a VGAM1839 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1839 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1839 precursor RNA is designated SEQ ID:1825, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1825 is located at position 139769 relative to the genome of Fowlpox Virus.

[60979] VGAM1839 precursor RNA folds onto itself, forming VGAM1839 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60980] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1839 folded precursor RNA into VGAM1839 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1839 RNA is designated SEQ ID:4550, and is provided hereinbelow with reference to the sequence listing part.

[60981] VGAM1839 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1839 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1839 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[60982] VGAM1839 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1839 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1839 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1839 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1839 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60983] The complementary binding of VGAM1839 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1839 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1839 host target RNA into VGAM1839 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[60984] It is appreciated that VGAM1839 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1839 host target genes. The mRNA of each one of this plurality of VGAM1839 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1839 RNA, herein designated VGAM RNA, and which when bound by VGAM1839 RNA causes inhibition of translation of respective one or more VGAM1839 host target proteins.

[60985] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1839 gene, herein designated VGAM GENE, on one or more VGAM1839 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[60986] It is yet further appreciated that a function of VGAM1839 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1839 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1839 correlate with, and may be deduced from, the identity of the host target genes which VGAM1839 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[60987] Nucleotide sequences of the VGAM1839 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1839 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1839 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1839 are further described hereinbelow with reference to Table 1.

[60988] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1839 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1839 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[60989] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1839 gene, herein designated VGAM is inhibition of expression of VGAM1839 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1839 correlate with, and may be deduced from, the identity of the target genes which VGAM1839 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[60990] FLJ20051 (Accession NM\_019087) is a VGAM1839 host target gene. FLJ20051 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20051 BINDING SITE, designated SEQ ID:21163, to the nucleotide sequence of VGAM1839 RNA, herein designated VGAM RNA, also designated SEQ ID:4550.

[60991] A function of VGAM1839 is therefore inhibition of FLJ20051 (Accession NM\_019087). Accordingly, utilities of VGAM1839 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20051. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1840 (VGAM1840) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[60992] VGAM1840 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1840 was detected is described hereinabove with reference to Figs. 1–8.

[60993] VGAM1840 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpea Mottle Virus. VGAM1840 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[60994] VGAM1840 gene encodes a VGAM1840 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1840 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1840 precursor RNA is designated SEQ ID:1826, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1826 is located at position 998 relative to the genome of Cowpea Mottle Virus.

[60995] VGAM1840 precursor RNA folds onto itself, forming VGAM1840 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[60996] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1840 folded precursor RNA into VGAM1840 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1840 RNA is designated SEQ ID:4551, and is provided hereinbelow with reference to the sequence listing part.

[60997] VGAM1840 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1840 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1840 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[60998] VGAM1840 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1840 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1840 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1840 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1840 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[60999] The complementary binding of VGAM1840 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1840 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1840 host target RNA into VGAM1840 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61000] It is appreciated that VGAM1840 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1840 host target genes. The mRNA of each one of this plurality of VGAM1840 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1840 RNA, herein designated VGAM RNA, and which when bound by VGAM1840 RNA causes inhibition of translation of respective one or more VGAM1840 host target proteins.

[61001] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1840 gene, herein designated VGAM GENE, on one or more VGAM1840 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).



[61002] It is yet further appreciated that a function of VGAM1840 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1840 include diagnosis, prevention and treatment of viral infection by Cowpea Mottle Virus. Specific functions, and accordingly utilities, of VGAM1840 correlate with, and may be deduced from, the identity of the host target genes which VGAM1840 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61003] Nucleotide sequences of the VGAM1840 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1840 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1840 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1840 are further described hereinbelow with reference to Table 1.

[61004] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1840 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1840 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[61005] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1840 gene, herein designated VGAM is inhibition of expression of VGAM1840 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1840 correlate with, and may be deduced from, the identity of the target genes which VGAM1840 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61006] Testis Derived Transcript (3 LIM domains) (TES, Accession XM\_050430) is a VGAM1840 host target gene. TES BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TES, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TES BINDING SITE, designated SEQ ID:35632, to the nucleotide sequence of VGAM1840 RNA, herein designated VGAM RNA, also designated SEQ ID:4551.

[61007] A function of VGAM1840 is therefore inhibition of Testis Derived Transcript (3 LIM domains) (TES, Accession XM\_050430), a gene which acts as a tumor suppressor. Accordingly, utilities of VGAM1840 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with TES. The function of TES and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM363. Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM\_041375) is another VGAM1840 host target gene. C6orf37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf37 BINDING SITE, designated SEQ ID:33509, to the nucleotide sequence of VGAM1840 RNA, herein designated VGAM RNA, also designated SEQ ID:4551.

[61008] Another function of VGAM1840 is therefore inhibition of Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM\_041375). Accordingly, utilities of VGAM1840 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf37. SYNE-2 (Accession NM\_015180) is another VGAM1840 host target gene. SYNE-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

SYNE-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNE-2 BINDING SITE, designated SEQ ID:17534, to the nucleotide sequence of VGAM1840 RNA, herein designated VGAM RNA, also designated SEQ ID:4551.

[61009] Another function of VGAM1840 is therefore inhibition of SYNE-2 (Accession NM\_015180). Accordingly, utilities of VGAM1840 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNE-2. LOC121838 (Accession XM\_071772) is another VGAM1840 host target gene. LOC121838 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC121838, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121838 BINDING SITE, designated SEQ ID:37417, to the nucleotide sequence of VGAM1840 RNA, herein designated VGAM RNA, also designated SEQ ID:4551.

[61010] Another function of VGAM1840 is therefore inhibition of LOC121838 (Accession XM\_071772). Accordingly, utilities

of VGAM1840 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121838. LOC158337 (Accession XM\_098926) is another VGAM1840 host target gene. LOC158337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158337 BINDING SITE, designated SEQ ID:41960, to the nucleotide sequence of VGAM1840 RNA, herein designated VGAM RNA, also designated SEQ ID:4551.

[61011] Another function of VGAM1840 is therefore inhibition of LOC158337 (Accession XM\_098926). Accordingly, utilities of VGAM1840 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158337. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1841 (VGAM1841) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61012] VGAM1841 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1841 was detected is described hereinabove with reference to Figs. 1–8.

[61013] VGAM1841 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpea Mottle Virus. VGAM1841 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61014] VGAM1841 gene encodes a VGAM1841 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1841 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1841 precursor RNA is designated SEQ ID:1827, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1827 is located at position 695 relative to the genome of Cowpea Mottle Virus.

[61015] VGAM1841 precursor RNA folds onto itself, forming VGAM1841 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61016] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1841 folded precursor RNA into VGAM1841 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1841 RNA is designated SEQ ID:4552, and is provided hereinbelow with reference to the sequence listing part.

[61017] VGAM1841 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1841 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1841 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[61018] VGAM1841 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1841 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1841 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1841 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1841 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.



[61019] The complementary binding of VGAM1841 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1841 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1841 host target RNA into VGAM1841 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61020] It is appreciated that VGAM1841 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1841 host target genes. The mRNA of each one of this plurality of VGAM1841 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1841 RNA, herein designated VGAM RNA, and which when bound by VGAM1841 RNA causes inhibition of translation of respective one or more VGAM1841 host target proteins.

[61021] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1841 gene, herein designated VGAM GENE, on one or more VGAM1841 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61022] It is yet further appreciated that a function of VGAM1841 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of viral infection by Cowpea Mottle Virus. Specific functions, and accordingly utilities, of VGAM1841 correlate with, and may be deduced from, the identity of the host target genes which VGAM1841 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61023] Nucleotide sequences of the VGAM1841 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1841 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1841 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1841 are further  
described hereinbelow with reference to Table 1.

[61024] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1841 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1841 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[61025] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1841 gene, herein designated VGAM is  
inhibition of expression of VGAM1841 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1841 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1841  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[61026] Ankyrin Repeat Domain 3 (ANKRD3, Accession  
NM\_020639) is a VGAM1841 host target gene. ANKRD3

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKRD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKRD3 BINDING SITE, designated SEQ ID:21797, to the nucleotide sequence of VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61027] A function of VGAM1841 is therefore inhibition of Ankyrin Repeat Domain 3 (ANKRD3, Accession NM\_020639). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKRD3. Drebrin 1 (DBN1, Accession NM\_004395) is another VGAM1841 host target gene. DBN1 BINDING SITE1 and DBN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DBN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DBN1 BINDING SITE1 and DBN1 BINDING SITE2, designated SEQ ID:10638 and SEQ ID:28121 respectively, to the nucleotide sequence of

VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61028] Another function of VGAM1841 is therefore inhibition of Drebrin 1 (DBN1, Accession NM\_004395). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DBN1. Thrombomodulin (THBD, Accession NM\_000361) is another VGAM1841 host target gene. THBD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by THBD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THBD BINDING SITE, designated SEQ ID:5918, to the nucleotide sequence of VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61029] Another function of VGAM1841 is therefore inhibition of Thrombomodulin (THBD, Accession NM\_000361). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THBD. DKFZP727M111 (Accession NM\_015540) is another VGAM1841 host target gene. DKFZP727M111 BINDING SITE is HOST TARGET binding site found in the

5` untranslated region of mRNA encoded by DKFZP727M111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP727M111 BINDING SITE, designated SEQ ID:17800, to the nucleotide sequence of VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61030] Another function of VGAM1841 is therefore inhibition of DKFZP727M111 (Accession NM\_015540). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP727M111. KIAA0700 (Accession XM\_050561) is another VGAM1841 host target gene. KIAA0700 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0700 BINDING SITE, designated SEQ ID:35659, to the nucleotide sequence of VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61031] Another function of VGAM1841 is therefore inhibition of

KIAA0700 (Accession XM\_050561). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0700. LOC116166 (Accession XM\_007651) is another VGAM1841 host target gene. LOC116166 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116166 BINDING SITE, designated SEQ ID:30060, to the nucleotide sequence of VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61032] Another function of VGAM1841 is therefore inhibition of LOC116166 (Accession XM\_007651). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116166. LOC158987 (Accession XM\_099015) is another VGAM1841 host target gene. LOC158987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC158987 BINDING SITE, designated SEQ ID:42048, to the nucleotide sequence of VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61033] Another function of VGAM1841 is therefore inhibition of LOC158987 (Accession XM\_099015). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158987. LOC165904 (Accession XM\_093522) is another VGAM1841 host target gene. LOC165904 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC165904, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165904 BINDING SITE, designated SEQ ID:40195, to the nucleotide sequence of VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61034] Another function of VGAM1841 is therefore inhibition of LOC165904 (Accession XM\_093522). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165904. LOC90678 (Accession NM\_138361) is an-



other VGAM1841 host target gene. LOC90678 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90678 BINDING SITE, designated SEQ ID:28747, to the nucleotide sequence of VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61035] Another function of VGAM1841 is therefore inhibition of LOC90678 (Accession NM\_138361). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90678. LOC91807 (Accession XM\_040819) is another VGAM1841 host target gene. LOC91807 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91807, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91807 BINDING SITE, designated SEQ ID:33384, to the nucleotide sequence of VGAM1841 RNA, herein designated VGAM RNA, also designated SEQ ID:4552.

[61036] Another function of VGAM1841 is therefore inhibition of LOC91807 (Accession XM\_040819). Accordingly, utilities of VGAM1841 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91807. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1842 (VGAM1842) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61037] VGAM1842 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1842 was detected is described hereinabove with reference to Figs. 1-8.

[61038] VGAM1842 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1842 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61039] VGAM1842 gene encodes a VGAM1842 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1842 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1842 precursor RNA is designated SEQ ID:1828, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1828 is located at position 19726 relative to the genome of Chimpanzee Cytomegalovirus.

[61040] VGAM1842 precursor RNA folds onto itself, forming VGAM1842 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61041] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1842 folded precursor RNA into VGAM1842 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1842 RNA is designated SEQ ID:4553, and is provided hereinbelow with reference to the sequence listing part.

[61042] VGAM1842 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1842 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1842 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[61043] VGAM1842 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1842 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1842 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1842 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1842 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61044] The complementary binding of VGAM1842 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1842 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1842 host target RNA into VGAM1842 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61045] It is appreciated that VGAM1842 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1842 host target genes. The mRNA of each one of this plurality of VGAM1842 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1842 RNA, herein designated VGAM RNA, and which when bound by VGAM1842 RNA causes inhibition of translation of respective one or more VGAM1842 host target proteins.

[61046] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1842 gene, herein designated VGAM GENE, on one or more VGAM1842 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61047] It is yet further appreciated that a function of VGAM1842 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1842 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1842 correlate with, and may be deduced from, the identity of the host target genes which VGAM1842 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61048] Nucleotide sequences of the VGAM1842 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1842 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1842 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1842 are further described hereinbelow with reference to Table 1.

[61049] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1842 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1842 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[61050] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1842 gene, herein designated VGAM is inhibition of expression of VGAM1842 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1842 correlate with, and may be deduced from, the identity of the target genes which VGAM1842 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61051] Myelin Protein Zero (Charcot-Marie-Tooth neuropathy 1B) (MPZ, Accession NM\_000530) is a VGAM1842 host target gene. MPZ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPZ BINDING SITE, designated SEQ ID:6130, to the nucleotide sequence of VGAM1842 RNA, herein designated VGAM RNA, also designated SEQ ID:4553.

[61052] A function of VGAM1842 is therefore inhibition of Myelin Protein Zero (Charcot-Marie-Tooth neuropathy 1B) (MPZ, Accession NM\_000530). Accordingly, utilities of VGAM1842 include diagnosis, prevention and treatment



of diseases and clinical conditions associated with MPZ. LOC147080 (Accession XM\_097182) is another VGAM1842 host target gene. LOC147080 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147080, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147080 BINDING SITE, designated SEQ ID:40796, to the nucleotide sequence of VGAM1842 RNA, herein designated VGAM RNA, also designated SEQ ID:4553.

[61053] Another function of VGAM1842 is therefore inhibition of LOC147080 (Accession XM\_097182). Accordingly, utilities of VGAM1842 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147080. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1843 (VGAM1843) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61054] VGAM1843 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1843 was detected is described hereinabove with reference to Figs. 1-8.

[61055] VGAM1843 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1843 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61056] VGAM1843 gene encodes a VGAM1843 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1843 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1843 precursor RNA is designated SEQ ID:1829, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1829 is located at position 14213 relative to the genome of Chimpanzee Cytomegalovirus.

[61057] VGAM1843 precursor RNA folds onto itself, forming VGAM1843 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61058] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1843 folded precursor RNA into VGAM1843 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1843 RNA is designated SEQ ID:4554, and is provided hereinbelow with reference to the sequence listing part.

[61059] VGAM1843 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1843 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1843 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61060] VGAM1843 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1843 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1843 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1843 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1843 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61061] The complementary binding of VGAM1843 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1843 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1843 host target RNA into VGAM1843 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61062] It is appreciated that VGAM1843 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1843 host target genes. The mRNA of each one of this plurality of VGAM1843 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1843 RNA, herein designated VGAM RNA, and which when bound by VGAM1843 RNA causes inhibition of translation of respective one or more VGAM1843 host target proteins.

[61063] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1843 gene, herein designated VGAM GENE, on one or more VGAM1843 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61064] It is yet further appreciated that a function of VGAM1843 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1843 correlate with, and may be deduced from, the identity of the host target genes which VGAM1843 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61065] Nucleotide sequences of the VGAM1843 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1843 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1843 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1843 are further described hereinbelow with reference to Table 1.

[61066] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1843 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1843 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61067] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1843 gene, herein designated VGAM is inhibition of expression of VGAM1843 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1843 correlate with, and may be deduced from, the identity of the target genes which VGAM1843 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61068] Cytochrome P450, Subfamily IVF, Polypeptide 3 (leukotriene B4 omega hydroxylase) (CYP4F3, Accession NM\_000896) is a VGAM1843 host target gene. CYP4F3

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP4F3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP4F3 BINDING SITE, designated SEQ ID:6591, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61069] A function of VGAM1843 is therefore inhibition of Cytochrome P450, Subfamily IVF, Polypeptide 3 (leukotriene B4 omega hydroxylase) (CYP4F3, Accession NM\_000896), a gene which converts leukotriene B4 into the less active 20-hydroxy-leukotriene B4. Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP4F3. The function of CYP4F3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM186. Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM\_000109) is another VGAM1843 host target gene. DMD BINDING SITE1 through DMD BINDING SITE13 are HOST TARGET binding sites found in untranslated regions of



mRNA encoded by DMD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMD BINDING SITE1 through DMD BINDING SITE13, designated SEQ ID:5570, SEQ ID:10155, SEQ ID:10161, SEQ ID:10168, SEQ ID:10175, SEQ ID:10181, SEQ ID:10186, SEQ ID:10193, SEQ ID:10203, SEQ ID:10208, SEQ ID:10213, SEQ ID:10220 and SEQ ID:10232 respectively, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61070] Another function of VGAM1843 is therefore inhibition of Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM\_000109), a gene which muscular dystrophy . Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMD. The function of DMD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM218.Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome) (FGFR1, Accession NM\_023109) is another VGAM1843 host target

gene. FGFR1 BINDING SITE1 through FGFR1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGFR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGFR1 BINDING SITE1 through FGFR1 BINDING SITE3, designated SEQ ID:23372, SEQ ID:6207 and SEQ ID:6611 respectively, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61071] Another function of VGAM1843 is therefore inhibition of Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome) (FGFR1, Accession NM\_023109). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGFR1. Phosphoinositide-3-kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM\_002646) is another VGAM1843 host target gene. PIK3C2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3C2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of PIK3C2B BINDING SITE, designated SEQ ID:8508, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61072] Another function of VGAM1843 is therefore inhibition of Phosphoinositide-3-kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM\_002646). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3C2B. Regulator of G-protein Signalling 16 (RGS16, Accession NM\_002928) is another VGAM1843 host target gene. RGS16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGS16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS16 BINDING SITE, designated SEQ ID:8833, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61073] Another function of VGAM1843 is therefore inhibition of Regulator of G-protein Signalling 16 (RGS16, Accession NM\_002928), a gene which inhibits signal transduction.

Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS16. The function of RGS16 has been established by previous studies. Snow et al. (1998) found that the RGS16 gene contains 5 exons. Northern blot analysis revealed that RGS16 is expressed at high levels in retina and at lower levels in all other tissues examined. By searching for retinal-specific RGS family members that might be involved in the phototransduction cascade, Chen et al. (1996) identified cDNAs encoding the mouse and rat homologs of RGS16, called *Rgs-r* by them. Northern blot analysis showed that rat *Rgs16* is expressed predominantly in the retina. Chen et al. (1996) found that mouse *Rgs16* enhances the rate of GTP-hydrolysis by transducin (see OMIM Ref. No. GNAT2; 139340), suggesting that *Rgs16* may play a role in regulating the kinetics of signaling in the phototransduction cascade. The mouse and rat *Rgs16* proteins have 94% amino acid sequence identity. Snow et al. (1998) reported that the mouse and human RGS16 proteins have 86% amino acid sequence identity

[61074] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [61075] Snow, B. E.; Antonio, L.; Suggs, S.; Siderovski, D. P. : Cloning of a retinally abundant regulator of G-protein signaling (RGS-r/RGS16): genomic structure and chromosomal localization of the human gene. *Gene* 206: 247–253, 1998. ; and
- [61076] Chen, C.-K.; Wieland, T.; Simon, M. I. : RGS-r, a retinal specific RGS protein, binds an intermediate conformation of transducin and enhances recycling. *Proc. Nat. Acad. Sci.* 93: 12885–12888.
- [61077] Further studies establishing the function and utilities of RGS16 are found in John Hopkins OMIM database record ID 602514, and in cited publications numbered 8545–8548 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Selectin P Ligand (SELPLG, Accession XM\_006867) is another VGAM1843 host target gene. SELPLG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SELPLG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SELPLG BINDING SITE, designated SEQ ID:30019, to the nucleotide se-

quence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61078] Another function of VGAM1843 is therefore inhibition of Selectin P Ligand (SELPLG, Accession XM\_006867), a gene which binds to p-, e- and l-selectins, which mediates the tethering and rolling of neutrophils and t-lymphocytes on endothelial cells. Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SELPLG. The function of SELPLG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.Small Glutamine-rich Tetratricopeptide Repeat (TPR)-containing (SGT, Accession NM\_003021) is another VGAM1843 host target gene. SGT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SGT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SGT BINDING SITE, designated SEQ ID:8942, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61079] Another function of VGAM1843 is therefore inhibition of Small Glutamine-rich Tetratricopeptide Repeat (TPR)-containing (SGT, Accession NM\_003021). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SGT. Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 6 (SLC7A6, Accession NM\_003983) is another VGAM1843 host target gene. SLC7A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A6 BINDING SITE, designated SEQ ID:10130, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61080] Another function of VGAM1843 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 6 (SLC7A6, Accession NM\_003983), a gene which is involved in mediating amino acid transport. Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with SLC7A6. The function of SLC7A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM87.Tyrosinase-related Protein 1 (TYRP1, Accession XM\_051267) is another VGAM1843 host target gene.

TYRP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TYRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TYRP1 BINDING SITE, designated SEQ ID:35797, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61081] Another function of VGAM1843 is therefore inhibition of Tyrosinase-related Protein 1 (TYRP1, Accession XM\_051267). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TYRP1. Cytochrome P450, Subfamily IVF, Polypeptide 2 (CYP4F2, Accession NM\_001082) is another VGAM1843 host target gene. CYP4F2 BINDING SITE is HOST TARGET binding site found



in the 3` untranslated region of mRNA encoded by CYP4F2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP4F2 BINDING SITE, designated SEQ ID:6742, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61082] Another function of VGAM1843 is therefore inhibition of Cytochrome P450, Subfamily IVF, Polypeptide 2 (CYP4F2, Accession NM\_001082). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP4F2. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681) is another VGAM1843 host target gene. DDX34 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DDX34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE, designated SEQ ID:16161, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4554.

[61083] Another function of VGAM1843 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. DJ971N18.2 (Accession NM\_021156) is another VGAM1843 host target gene. DJ971N18.2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ971N18.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ971N18.2 BINDING SITE, designated SEQ ID:22135, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61084] Another function of VGAM1843 is therefore inhibition of DJ971N18.2 (Accession NM\_021156). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ971N18.2. DKFZp547M072 (Accession XM\_028067) is another VGAM1843 host target gene. DKFZp547M072 BINDING SITE is HOST TARGET binding site found in the

3' untranslated region of mRNA encoded by DKFZp547M072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547M072 BINDING SITE, designated SEQ ID:30615, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61085] Another function of VGAM1843 is therefore inhibition of DKFZp547M072 (Accession XM\_028067). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547M072. DKFZP586M1120 (Accession NM\_031294) is another VGAM1843 host target gene. DKFZP586M1120 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586M1120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586M1120 BINDING SITE, designated SEQ ID:25322, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61086] Another function of VGAM1843 is therefore inhibition of DKFZP586M1120 (Accession NM\_031294). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586M1120. FLJ10751 (Accession NM\_018205) is another VGAM1843 host target gene. FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10751, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2, designated SEQ ID:20092 and SEQ ID:20191 respectively, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61087] Another function of VGAM1843 is therefore inhibition of FLJ10751 (Accession NM\_018205). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10751. KIAA0342 (Accession XM\_047357) is another VGAM1843 host target gene. KIAA0342 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by KIAA0342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0342 BINDING SITE, designated SEQ ID:34959, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61088] Another function of VGAM1843 is therefore inhibition of KIAA0342 (Accession XM\_047357). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0342. KIAA0478 (Accession NM\_014870) is another VGAM1843 host target gene. KIAA0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0478 BINDING SITE, designated SEQ ID:16978, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61089] Another function of VGAM1843 is therefore inhibition of KIAA0478 (Accession NM\_014870). Accordingly, utilities

of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0478. KIAA1332 (Accession XM\_048774) is another VGAM1843 host target gene. KIAA1332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1332 BINDING SITE, designated SEQ ID:35256, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61090] Another function of VGAM1843 is therefore inhibition of KIAA1332 (Accession XM\_048774). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1332. KIAA1529 (Accession XM\_047336) is another VGAM1843 host target gene. KIAA1529 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1529 BINDING SITE, designated SEQ ID:34951, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61091] Another function of VGAM1843 is therefore inhibition of KIAA1529 (Accession XM\_047336). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1529. KIAA1674 (Accession XM\_044065) is another VGAM1843 host target gene. KIAA1674 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1674, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1674 BINDING SITE, designated SEQ ID:34112, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61092] Another function of VGAM1843 is therefore inhibition of KIAA1674 (Accession XM\_044065). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1674. KIAA1679 (Accession XM\_046570) is another VGAM1843 host target gene. KIAA1679 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1679, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1679 BINDING SITE, designated SEQ ID:34751, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61093] Another function of VGAM1843 is therefore inhibition of KIAA1679 (Accession XM\_046570). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1679. KIAA1878 (Accession XM\_166256) is another VGAM1843 host target gene. KIAA1878 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1878, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1878 BINDING SITE, designated SEQ ID:44075, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61094] Another function of VGAM1843 is therefore inhibition of



KIAA1878 (Accession XM\_166256). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1878. Serine/threonine Kinase 38 Like (STK38L, Accession XM\_044823) is another VGAM1843 host target gene. STK38L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK38L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK38L BINDING SITE, designated SEQ ID:34290, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61095] Another function of VGAM1843 is therefore inhibition of Serine/threonine Kinase 38 Like (STK38L, Accession XM\_044823). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK38L. LOC139248 (Accession XM\_066582) is another VGAM1843 host target gene. LOC139248 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC139248, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139248 BINDING SITE, designated SEQ ID:37335, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61096] Another function of VGAM1843 is therefore inhibition of LOC139248 (Accession XM\_066582). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139248. LOC145225 (Accession XM\_096741) is another VGAM1843 host target gene. LOC145225 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145225, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145225 BINDING SITE, designated SEQ ID:40526, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61097] Another function of VGAM1843 is therefore inhibition of LOC145225 (Accession XM\_096741). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC145225. LOC146756 (Accession XM\_097085) is another VGAM1843 host target gene. LOC146756 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146756, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146756 BINDING SITE, designated SEQ ID:40736, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61098] Another function of VGAM1843 is therefore inhibition of LOC146756 (Accession XM\_097085). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146756. LOC148229 (Accession XM\_086103) is another VGAM1843 host target gene. LOC148229 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148229 BINDING SITE, designated SEQ ID:38497, to

the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61099] Another function of VGAM1843 is therefore inhibition of LOC148229 (Accession XM\_086103). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148229. LOC166867 (Accession XM\_094142) is another VGAM1843 host target gene. LOC166867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC166867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166867 BINDING SITE, designated SEQ ID:40222, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61100] Another function of VGAM1843 is therefore inhibition of LOC166867 (Accession XM\_094142). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166867. LOC196510 (Accession XM\_113738) is another VGAM1843 host target gene. LOC196510 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC196510, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196510 BINDING SITE, designated SEQ ID:42395, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61101] Another function of VGAM1843 is therefore inhibition of LOC196510 (Accession XM\_113738). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196510. LOC200220 (Accession XM\_114157) is another VGAM1843 host target gene. LOC200220 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200220 BINDING SITE, designated SEQ ID:42744, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61102] Another function of VGAM1843 is therefore inhibition of LOC200220 (Accession XM\_114157). Accordingly, utilities

of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200220. LOC200310 (Accession XM\_037840) is another VGAM1843 host target gene. LOC200310 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200310 BINDING SITE, designated SEQ ID:32708, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61103] Another function of VGAM1843 is therefore inhibition of LOC200310 (Accession XM\_037840). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200310. LOC201952 (Accession XM\_117345) is another VGAM1843 host target gene. LOC201952 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201952, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC201952 BINDING SITE, designated SEQ ID:43394, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61104] Another function of VGAM1843 is therefore inhibition of LOC201952 (Accession XM\_117345). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201952. LOC202934 (Accession XM\_117486) is another VGAM1843 host target gene. LOC202934 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202934 BINDING SITE, designated SEQ ID:43459, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61105] Another function of VGAM1843 is therefore inhibition of LOC202934 (Accession XM\_117486). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202934. LOC219627 (Accession XM\_166402) is another VGAM1843 host target gene. LOC219627 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219627 BINDING SITE, designated SEQ ID:44274, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61106] Another function of VGAM1843 is therefore inhibition of LOC219627 (Accession XM\_166402). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219627. LOC219848 (Accession XM\_166170) is another VGAM1843 host target gene. LOC219848 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219848 BINDING SITE, designated SEQ ID:43986, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61107] Another function of VGAM1843 is therefore inhibition of



LOC219848 (Accession XM\_166170). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219848. LOC222066 (Accession XM\_166582) is another VGAM1843 host target gene. LOC222066 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222066, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222066 BINDING SITE, designated SEQ ID:44556, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61108] Another function of VGAM1843 is therefore inhibition of LOC222066 (Accession XM\_166582). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222066. LOC222962 (Accession XM\_167291) is another VGAM1843 host target gene. LOC222962 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC222962 BINDING SITE, designated SEQ ID:44629, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61109] Another function of VGAM1843 is therefore inhibition of LOC222962 (Accession XM\_167291). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222962. LOC254015 (Accession XM\_172977) is another VGAM1843 host target gene. LOC254015 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254015 BINDING SITE, designated SEQ ID:46244, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61110] Another function of VGAM1843 is therefore inhibition of LOC254015 (Accession XM\_172977). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254015. LOC254778 (Accession XM\_171193) is an-

other VGAM1843 host target gene. LOC254778 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254778, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254778 BINDING SITE, designated SEQ ID:45977, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61111] Another function of VGAM1843 is therefore inhibition of LOC254778 (Accession XM\_171193). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254778. LOC255465 (Accession XM\_173206) is another VGAM1843 host target gene. LOC255465 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255465 BINDING SITE, designated SEQ ID:46452, to the nucleotide sequence of VGAM1843 RNA, herein designated VGAM RNA, also designated SEQ ID:4554.

[61112] Another function of VGAM1843 is therefore inhibition of LOC255465 (Accession XM\_173206). Accordingly, utilities of VGAM1843 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255465. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1844 (VGAM1844) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61113] VGAM1844 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1844 was detected is described hereinabove with reference to Figs. 1-8.

[61114] VGAM1844 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1844 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61115] VGAM1844 gene encodes a VGAM1844 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1844 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1844 precursor RNA is designated SEQ ID:1830, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1830 is located at position 20461 relative to the genome of Chimpanzee Cytomegalovirus.

- [61116] VGAM1844 precursor RNA folds onto itself, forming VGAM1844 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [61117] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1844 folded precursor RNA into VGAM1844 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1844 RNA is designated SEQ ID:4555, and is provided hereinbelow with reference to the sequence listing part.

[61118] VGAM1844 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1844 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1844 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61119] VGAM1844 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1844 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1844 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1844 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1844 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61120] The complementary binding of VGAM1844 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1844 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1844 host target RNA into VGAM1844 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61121] It is appreciated that VGAM1844 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1844 host target genes. The mRNA of each one of this plurality of VGAM1844 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1844 RNA, herein designated VGAM RNA, and which when bound by VGAM1844 RNA causes inhibition of translation of respective one or more VGAM1844 host target proteins.

[61122] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1844 gene, herein designated VGAM GENE, on one or more VGAM1844 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).



[61123] It is yet further appreciated that a function of VGAM1844 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1844 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1844 correlate with, and may be deduced from, the identity of the host target genes which VGAM1844 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61124] Nucleotide sequences of the VGAM1844 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1844 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1844 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1844 are further described hereinbelow with reference to Table 1.

[61125] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1844 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1844 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[61126] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1844 gene, herein designated VGAM is inhibition of expression of VGAM1844 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1844 correlate with, and may be deduced from, the identity of the target genes which VGAM1844 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61127] Alpha-methylacyl-CoA Racemase (AMACR, Accession XM\_043771) is a VGAM1844 host target gene. AMACR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMACR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMACR BINDING SITE, designated SEQ ID:34014, to the nucleotide sequence of VGAM1844 RNA, herein designated VGAM RNA, also designated SEQ ID:4555.

[61128] A function of VGAM1844 is therefore inhibition of Alpha-methylacyl-CoA Racemase (AMACR, Accession XM\_043771). Accordingly, utilities of VGAM1844 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with AMACR. KIAA1305 (Accession NM\_025081) is another VGAM1844 host target gene. KIAA1305 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1305 BINDING SITE, designated SEQ ID:24683, to the nucleotide sequence of VGAM1844 RNA, herein designated VGAM RNA, also designated SEQ ID:4555.

[61129] Another function of VGAM1844 is therefore inhibition of KIAA1305 (Accession NM\_025081). Accordingly, utilities of VGAM1844 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1305. LOC145547 (Accession XM\_085167) is another VGAM1844 host target gene. LOC145547 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145547 BINDING SITE, designated SEQ ID:37894, to

the nucleotide sequence of VGAM1844 RNA, herein designated VGAM RNA, also designated SEQ ID:4555.

[61130] Another function of VGAM1844 is therefore inhibition of LOC145547 (Accession XM\_085167). Accordingly, utilities of VGAM1844 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145547. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1845 (VGAM1845) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61131] VGAM1845 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1845 was detected is described hereinabove with reference to Figs. 1–8.

[61132] VGAM1845 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1845 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61133] VGAM1845 gene encodes a VGAM1845 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1845 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1845 precursor RNA is designated SEQ ID:1831, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1831 is located at position 23567 relative to the genome of Chimpanzee Cytomegalovirus.

- [61134] VGAM1845 precursor RNA folds onto itself, forming VGAM1845 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [61135] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1845 folded precursor RNA into VGAM1845 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1845 RNA is designated SEQ ID:4556, and is provided hereinbelow with reference to the sequence listing part.

[61136] VGAM1845 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1845 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1845 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61137] VGAM1845 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1845 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1845 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1845 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1845 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61138] The complementary binding of VGAM1845 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1845 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1845 host target RNA into VGAM1845 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61139] It is appreciated that VGAM1845 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1845 host target genes. The mRNA of each one of this plurality of VGAM1845 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1845 RNA, herein designated VGAM RNA, and which when bound by VGAM1845 RNA causes inhibition of translation of respective one or more VGAM1845 host target proteins.

[61140] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1845 gene, herein designated VGAM GENE, on one or more VGAM1845 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[61141] It is yet further appreciated that a function of VGAM1845 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cy-tomegalovirus. Specific functions, and accordingly utilities, of VGAM1845 correlate with, and may be deduced from, the identity of the host target genes which VGAM1845 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61142] Nucleotide sequences of the VGAM1845 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1845 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1845 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1845 are further described hereinbelow with reference to Table 1.

[61143] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1845 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1845 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61144] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1845 gene, herein designated VGAM is inhibition of expression of VGAM1845 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1845 correlate with, and may be deduced from, the identity of the target genes which VGAM1845 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61145] CD3Z Antigen, Zeta Polypeptide (TiT3 complex) (CD3Z, Accession NM\_000734) is a VGAM1845 host target gene. CD3Z BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD3Z, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD3Z BINDING SITE, designated SEQ ID:6391, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61146] A function of VGAM1845 is therefore inhibition of CD3Z Antigen, Zeta Polypeptide (TiT3 complex) (CD3Z, Acces-

sion NM\_000734), a gene which may involve in assembly and expression of the tcr complex as well as signal transduction upon antigen triggering. Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD3Z. The function of CD3Z and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM167. Chemokine (C-X-C motif) Ligand 16 (CXCL16, Accession NM\_022059) is another VGAM1845 host target gene. CXCL16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXCL16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXCL16 BINDING SITE, designated SEQ ID:22596, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61147] Another function of VGAM1845 is therefore inhibition of Chemokine (C-X-C motif) Ligand 16 (CXCL16, Accession NM\_022059), a gene which induces calcium mobilization. Accordingly, utilities of VGAM1845 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with CXCL16. The function of CXCL16 has been established by previous studies. Using a 2-step EST database search in which putative transcripts were scanned for the occurrence of functional patterns, Matloubian et al. (2000) identified a cDNA encoding a CXC chemokine that they termed CXCL16. The predicted 273-amino acid CXCL16 protein, which is 49% identical to the 246-amino acid mouse sequence, contains a non-glu/leu/arg (ELR) motif-containing CXC chemokine domain, a mucin-like spacer region, a transmembrane domain, and a cytoplasmic tail with a potential tyrosine phosphorylation and SH2 protein-binding site. CXCL16 was the first transmembrane CXC chemokine identified; CX3CL1 (SCYD1; 601880), which also has a mucin-like spacer region, was the only other known transmembrane chemokine. Northern blot analysis of mouse and human tissues detected a 2.2-kb CXCL16 transcript in spleen, lymph nodes, Peyer patches, lung, kidney, small intestine, and thymus, with weak expression in heart and liver and no expression in brain and bone marrow. Flow cytometry and Western blot analysis demonstrated expression of an approximately 60-kD glycosylated cell-surface protein as

well as a cell supernatant 35-kD soluble protein. Flow cytometry of cells from mouse tissues indicated that CXCL16 is found on CD11C (ITGAX; 151510)-positive splenic and lymph node dendritic cells; this expression was increased after injection with lipopolysaccharide. Immunohistochemical analysis showed that CXCL16 is expressed in T-cell areas of the splenic white pulp, lymph nodes, the thymus medulla, and, interestingly, in the splenic red pulp. No staining was observed in B-cell areas. After injection of inflammatory mediators, expression was enhanced in T-cell zones and, more prominently, in splenic red pulp. Chemotaxis assays found that CXCL16 induced a strong chemotactic response in activated CD8 T cells. In addition, CXCL16 induced calcium mobilization. Expression cloning of mouse Cxcl16 identified a protein with 71% amino acid identity to human BONZO (OMIM Ref. No. 605163), which Matloubian et al. (2000) renamed CXCR6. Human and mouse cells expressing CXCR6 showed a strong chemotactic response to CXCL16 but not to other chemokines. The authors concluded that CXCL16 and CXCR6 probably function in interactions between dendritic cells and T cells and in regulating T-cell migration in the splenic red pulp. Macrophages endocytose oxi-

dized low density lipoprotein (OxLDL) by a receptor-mediated mechanism. By expression cloning from a phorbol ester-stimulated THP-1 cell library, Shimaoka et al. (2000) isolated a cDNA encoding SRPSOX (scavenger receptor that binds phosphatidylserine and oxidized lipoprotein). The deduced 254-amino acid type I transmembrane protein is identical to the CXCL16 protein reported by Matloubian et al. (2000) except that SRPSOX differs by 2 residues and lacks the N-terminal 19 amino acids. Cells expressing SRPSOX bound to phosphatidylserine-coated plates; this binding could be inhibited by OxLDL. Scatchard analysis confirmed that SRPSOX is a specific receptor for OxLDL but not LDL or acetyl-LDL. Fluorescence microscopy demonstrated OxLDL uptake in SRPSOX-expressing cells. Immunoblot analysis showed that SRPSOX is expressed as a 30-kD protein in human and mouse macrophages. Northern blot analysis revealed differentiation-inducible expression of 1.8- and 2.5-kb transcripts in macrophages.

[61148] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[61149] Matloubian, M.; David, A.; Engel, S.; Ryan, J. E.; Cyster, J.

G. : A transmembrane CXC chemokine is a ligand for HIV-coreceptor Bonzo. Nature Immun. 1: 298–304, 2000. ;  
and

[61150] Shimaoka, T.; Kume, N.; Minami, M.; Hayashida, K.; Kataoka, H.; Kita, T.; Yonehara, S. : Molecular cloning of a novel scavenger receptor for oxidized low density lipoprotein, SR-PSOX.

[61151] Further studies establishing the function and utilities of CXCL16 are found in John Hopkins OMIM database record ID 605398, and in cited publications numbered 439 and 7313–7314 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Huntingtin-associated Protein 1 (neuroan 1) (HAP1, Accession NM\_003949) is another VGAM1845 host target gene. HAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HAP1 BINDING SITE, designated SEQ ID:10074, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61152] Another function of VGAM1845 is therefore inhibition of

Huntingtin-associated Protein 1 (neuroan 1) (HAP1, Accession NM\_003949), a gene which functions as an adaptor protein using coiled coils to mediate interactions among cytoskeletal, vascular, and motor proteins. Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HAP1. The function of HAP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM126. Polymeric Immunoglobulin Receptor (PIGR, Accession XM\_052013) is another VGAM1845 host target gene. PIGR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIGR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIGR BINDING SITE, designated SEQ ID:35936, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61153] Another function of VGAM1845 is therefore inhibition of Polymeric Immunoglobulin Receptor (PIGR, Accession XM\_052013). Accordingly, utilities of VGAM1845 include



diagnosis, prevention and treatment of diseases and clinical conditions associated with PIGR. Proteoglycan 2, Bone Marrow (natural killer cell activator, eosinophil granule major basic protein) (PRG2, Accession NM\_002728) is another VGAM1845 host target gene. PRG2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRG2 BINDING SITE, designated SEQ ID:8592, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61154] Another function of VGAM1845 is therefore inhibition of Proteoglycan 2, Bone Marrow (natural killer cell activator, eosinophil granule major basic protein) (PRG2, Accession NM\_002728), a gene which Myelin basic protein; a constituent of myelin, plays a role in nerve function. Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRG2. The function of PRG2 has been established by previous studies. Eosinophil granule major basic protein (MBP) comprises the crystalloid core of the

eosinophil granule. Wasmoen et al. (1988) and Weller et al. (1988) published a partial amino acid sequence for MBP, also designated proteoglycan-2 (PRG2). Using this partial sequence, Barker et al. (1988) isolated a full-length PRG2 cDNA from a human promyelocytic leukemia cell line (HL60) cDNA library. McGrogan et al. (1988) independently isolated a PRG2 cDNA from an HL60 cell line cDNA. Yoshimatsu et al. (1992) also identified PRG2 in a search for a natural killer (NK) cell-activating factor purified from the supernatant of a T-cell hybridoma. McGrogan et al. (1988) and Barker et al. (1988) determined that the PRG2 cDNA encodes a deduced 222-amino acid protein with a 15-amino acid hydrophobic signal sequence. PRG2 is initially translated as a 25-kD preproprotein that is post-translationally modified to a proprotein. Posttranslational modification results in the mature form of PRG2, which is encoded by the carboxy 117 amino acids of the preproprotein and has a molecular mass of 14 kD. The 90-amino acid N-terminal domain has 1 potential N-linked glycosylation site. Yoshimatsu et al. (1992) reported that the C-terminal end of PRG2 shares homology with animal lectins. McGrogan et al. (1988) determined that the putative PRG2 proprotein is a bipolar molecule. The amino-

terminal half is hydrophilic, whereas the mature PRG2 is hydrophobic. Barker et al. (1988) hypothesized that the translation of PRG2 as a bipolar proprotein may mask the toxic effects of the mature PRG2 and protect the eosinophil from damage while the protein is processed through the endoplasmic reticulum to its sequestered site in the eosinophil granule. Using Northern blot analysis, McGrogan et al. (1988) detected a major 1-kb transcript and a minor 0.5-kb PRG2 transcript in HL60 cells. By the same method, Li et al. (1995) detected a 1-kb transcript in immature cells including bone-marrow and HL60 cells, but not in purified blood eosinophils. Using RT-PCR, Li et al. (1995) detected an additional 1.6-kb transcript in bone marrow cells and HL60 cells at lower levels than the 1-kb transcript. In differentiated blood eosinophils from idiopathic hypereosinophilic syndrome patients, the 1.6-kb transcript predominated. The International Radiation Hybrid Mapping Consortium mapped the PRG2 gene to chromosome 11 (A005W41). By FISH, Plager et al. (2001) mapped the PRG2 and PRG3 (OMIM Ref. No. 606814) genes to chromosome 11cen-q12.

[61155] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

[61156] Li, M.-S.; Sun, L.; Satoh, T.; Fisher, L. M.; Spry, C. J. F. :

Human eosinophil major basic protein, a mediator of allergic inflammation, is expressed by alternative splicing from two promoters. *Biochem. J.* 305: 921–927, 1995. ; and

[61157] Plager, D. A.; Weiler, D. A.; Loegering, D. A.; Johnson, W. B.; Haley, L.; Eddy, R. L.; Shows, T. B.; Gleich, G. J. : Comparative structure, proximal promoter elements, and chromosome lo.

[61158] Further studies establishing the function and utilities of PRG2 are found in John Hopkins OMIM database record ID 605601, and in cited publications numbered 6995–7001 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pleckstrin and Sec7 Domain Protein (PSD, Accession NM\_002779) is another VGAM1845 host target gene. PSD BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PSD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSD BINDING SITE, designated SEQ ID:8670, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4556.

[61159] Another function of VGAM1845 is therefore inhibition of Pleckstrin and Sec7 Domain Protein (PSD, Accession NM\_002779), a gene which promotes guanine–nucleotide exchange on arf6. Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSD. The function of PSD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM261.Prostaglandin I<sub>2</sub> (prostacyclin) Synthase (PTGIS, Accession NM\_000961) is another VGAM1845 host target gene. PTGIS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGIS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGIS BINDING SITE, designated SEQ ID:6666, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61160] Another function of VGAM1845 is therefore inhibition of Prostaglandin I<sub>2</sub> (prostacyclin) Synthase (PTGIS, Accession NM\_000961), a gene which catalyzes the isomerization of

prostaglandin h2 to prostacyclin (= prostaglandin i2). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGIS. The function of PTGIS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Solute Carrier Family 22 (organic anion/cation transporter), Member 12 (SLC22A12, Accession NM\_144585) is another VGAM1845 host target gene. SLC22A12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC22A12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC22A12 BINDING SITE, designated SEQ ID:29403, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61161] Another function of VGAM1845 is therefore inhibition of Solute Carrier Family 22 (organic anion/cation transporter), Member 12 (SLC22A12, Accession NM\_144585), a gene which is a urate -anion exchanger regulating blood urate levels. Accordingly, utilities of VGAM1845 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC22A12. The function of SLC22A12 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1034.Unc-13-like (*C. elegans*) (UNC13, Accession NM\_006377) is another VGAM1845 host target gene. UNC13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UNC13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UNC13 BINDING SITE, designated SEQ ID:13069, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61162] Another function of VGAM1845 is therefore inhibition of Unc-13-like (*C. elegans*) (UNC13, Accession NM\_006377), a gene which is a putative diacylglycerol receptor and may act in PKC-independent, diacylglycerol-activated apoptosis pathway. Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNC13. The function of



UNC13 has been established by previous studies. The priming step of synaptic vesicle exocytosis is thought to require the formation of the SNARE complex, which comprises the proteins synaptobrevin (OMIM Ref. No. 185881), SNAP25 (OMIM Ref. No. 600322), and syntaxin (see OMIM Ref. No. 186590). In solution, syntaxin adopts a default, closed configuration that is incompatible with formation of the SNARE complex. Specifically, the amino terminus of syntaxin binds the SNARE motif and occludes interactions with the other SNARE proteins. The N terminus of syntaxin also binds the presynaptic protein UNC13. Studies in mouse, *Drosophila*, and *Caenorhabditis elegans* suggest that UNC13 functions at a post-docking step of exocytosis, most likely during synaptic vesicle priming. Therefore, UNC13 binding to the N terminus of syntaxin may promote the open configuration of syntaxin. To test this model, Richmond et al. (2001) engineered mutations into *C. elegans* syntaxin that caused the protein to adopt the open configuration constitutively. Richmond et al. (2001) demonstrated that the open form of syntaxin can bypass the requirement for UNC13 in synaptic vesicle priming. Thus, Richmond et al. (2001) concluded that it is likely that UNC13 primes synaptic vesicles for fusion by

promoting the open configuration of syntaxin. Animal model experiments lend further support to the function of UNC13. Munc13-1 is a presynaptic protein with an essential role in synaptic vesicle priming. It contains a diacylglycerol (DAG)/beta phorbol ester-binding C1 domain and is a potential target of the DAG second messenger pathway that may act in parallel with protein kinases C (PKCs; OMIM Ref. No. 600448). Using genetically modified mice that expressed a DAG/beta phorbol ester-binding-deficient Munc13-1 variant (missense mutation his567 to lys) instead of the wildtype protein, Rhee et al. (2002) determined the relative contribution of PKCs and Munc13-1 to DAG/beta phorbol ester-dependent regulation of neurotransmitter release. They showed that Munc13s are the main presynaptic DAG/beta phorbol ester receptors in hippocampal neurons. Modulation of Munc13-1 activity by second messengers via the DAG/beta phorbol ester-binding C1 domain is essential for use-dependent alterations of synaptic efficacy and survival.

[61163] It is appreciated that the abovementioned animal model for UNC13 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appre-

ciated from the publications sited hereinbelow.

[61164] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[61165] Richmond, J. E.; Weimer, R. M.; Jorgensen, E. M. : An open form of syntaxin bypasses the requirement for UNC-13 in vesicle priming. *Nature* 412: 338–341, 2001. ; and

[61166] Rhee, J.-S.; Betz, A.; Pyott, S.; Reim, K.; Varoqueaux, F.; Augustin, I.; Hesse, D.; Sudhof, T. C.; Takahashi, M.; Rosenmund, C.; Brose, N. : Beta phorbol ester- and diacylglycerol-indu.

[61167] Further studies establishing the function and utilities of UNC13 are found in John Hopkins OMIM database record ID 605836, and in sited publications numbered 6430–6432, 176 and 6433–6434 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. V–yes–1 Yamaguchi Sarcoma Viral Oncogene Homolog 1 (YES1, Accession NM\_005433) is another VGAM1845 host target gene. YES1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by YES1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com–

plementarity of the nucleotide sequences of YES1 BINDING SITE, designated SEQ ID:11911, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61168] Another function of VGAM1845 is therefore inhibition of V–yes–1 Yamaguchi Sarcoma Viral Oncogene Homolog 1 (YES1, Accession NM\_005433), a gene which is a putative protein–tyrosine kinase. Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YES1. The function of YES1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.Zinc Finger Protein 137 (clone pHZ–30) (ZNF137, Accession NM\_003438) is another VGAM1845 host target gene. ZNF137 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF137, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF137 BINDING SITE, designated SEQ ID:9492, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also des–

ignated SEQ ID:4556.

[61169] Another function of VGAM1845 is therefore inhibition of Zinc Finger Protein 137 (clone pHZ-30) (ZNF137, Accession NM\_003438). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF137. APCL (Accession NM\_005883) is another VGAM1845 host target gene. APCL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APCL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APCL BINDING SITE, designated SEQ ID:12501, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61170] Another function of VGAM1845 is therefore inhibition of APCL (Accession NM\_005883). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APCL. Chromosome 11 Open Reading Frame 17 (C11orf17, Accession NM\_020642) is another VGAM1845 host target gene. C11orf17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by C11orf17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf17 BINDING SITE, designated SEQ ID:21806, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61171] Another function of VGAM1845 is therefore inhibition of Chromosome 11 Open Reading Frame 17 (C11orf17, Accession NM\_020642). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf17. Carcinoembryonic Antigen-related Cell Adhesion Molecule 8 (CEACAM8, Accession NM\_001816) is another VGAM1845 host target gene. CEACAM8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CEACAM8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEACAM8 BINDING SITE, designated SEQ ID:7560, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61172] Another function of VGAM1845 is therefore inhibition of Carcinoembryonic Antigen-related Cell Adhesion Molecule 8 (CEACAM8, Accession NM\_001816). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEACAM8. DKFZP434P0111 (Accession XM\_041116) is another VGAM1845 host target gene. DKFZP434P0111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P0111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P0111 BINDING SITE, designated SEQ ID:33456, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61173] Another function of VGAM1845 is therefore inhibition of DKFZP434P0111 (Accession XM\_041116). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0111. DKFZP566G1424 (Accession XM\_097771) is another VGAM1845 host target gene. DKFZP566G1424 BINDING SITE is HOST TARGET binding site

found in the 5` untranslated region of mRNA encoded by DKFZP566G1424, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566G1424 BINDING SITE, designated SEQ ID:41113, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61174] Another function of VGAM1845 is therefore inhibition of DKFZP566G1424 (Accession XM\_097771). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566G1424. FLJ14442 (Accession NM\_032785) is another VGAM1845 host target gene. FLJ14442 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14442 BINDING SITE, designated SEQ ID:26538, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61175] Another function of VGAM1845 is therefore inhibition of



FLJ14442 (Accession NM\_032785). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14442. FLJ20291 (Accession NM\_017748) is another VGAM1845 host target gene. FLJ20291 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20291, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20291 BINDING SITE, designated SEQ ID:19340, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61176] Another function of VGAM1845 is therefore inhibition of FLJ20291 (Accession NM\_017748). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20291. FLJ23556 (Accession NM\_024880) is another VGAM1845 host target gene. FLJ23556 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of FLJ23556 BINDING SITE, designated SEQ ID:24319, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61177] Another function of VGAM1845 is therefore inhibition of FLJ23556 (Accession NM\_024880). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23556. KIAA0720 (Accession XM\_030970) is another VGAM1845 host target gene. KIAA0720 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0720 BINDING SITE, designated SEQ ID:31236, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61178] Another function of VGAM1845 is therefore inhibition of KIAA0720 (Accession XM\_030970). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0720. KIAA1615 (Accession XM\_044021) is another

VGAM1845 host target gene. KIAA1615 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1615, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1615 BINDING SITE, designated SEQ ID:34087, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61179] Another function of VGAM1845 is therefore inhibition of KIAA1615 (Accession XM\_044021). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1615. KIAA1727 (Accession XM\_034262) is another VGAM1845 host target gene. KIAA1727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1727 BINDING SITE, designated SEQ ID:32035, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61180] Another function of VGAM1845 is therefore inhibition of KIAA1727 (Accession XM\_034262). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1727. KIAA1877 (Accession XM\_038616) is another VGAM1845 host target gene. KIAA1877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1877 BINDING SITE, designated SEQ ID:32880, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61181] Another function of VGAM1845 is therefore inhibition of KIAA1877 (Accession XM\_038616). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1877. KIAA1924 (Accession XM\_057091) is another VGAM1845 host target gene. KIAA1924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1924, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1924 BINDING SITE, designated SEQ ID:36472, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61182] Another function of VGAM1845 is therefore inhibition of KIAA1924 (Accession XM\_057091). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1924. Nup43 (Accession NM\_024647) is another VGAM1845 host target gene. Nup43 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Nup43, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Nup43 BINDING SITE, designated SEQ ID:23935, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61183] Another function of VGAM1845 is therefore inhibition of Nup43 (Accession NM\_024647). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Nup43.

Phytanoyl-CoA Hydroxylase Interacting Protein (PHYHIP, Accession NM\_014759) is another VGAM1845 host target gene. PHYHIP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PHYHIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHYHIP BINDING SITE, designated SEQ ID:16510, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61184] Another function of VGAM1845 is therefore inhibition of Phytanoyl-CoA Hydroxylase Interacting Protein (PHYHIP, Accession NM\_014759). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHYHIP. PRO1992 (Accession NM\_014107) is another VGAM1845 host target gene. PRO1992 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO1992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1992 BINDING SITE,

designated SEQ ID:15334, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61185] Another function of VGAM1845 is therefore inhibition of PRO1992 (Accession NM\_014107). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1992. RAP140 (Accession NM\_015224) is another VGAM1845 host target gene. RAP140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP140 BINDING SITE, designated SEQ ID:17552, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61186] Another function of VGAM1845 is therefore inhibition of RAP140 (Accession NM\_015224). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAP140. LOC121504 (Accession XM\_058571) is another VGAM1845 host target gene. LOC121504 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC121504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121504 BINDING SITE, designated SEQ ID:36670, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61187] Another function of VGAM1845 is therefore inhibition of LOC121504 (Accession XM\_058571). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121504. LOC128077 (Accession XM\_059208) is another VGAM1845 host target gene. LOC128077 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128077 BINDING SITE, designated SEQ ID:36915, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61188] Another function of VGAM1845 is therefore inhibition of



LOC128077 (Accession XM\_059208). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128077. LOC146909 (Accession XM\_085634) is another VGAM1845 host target gene. LOC146909 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146909, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146909 BINDING SITE, designated SEQ ID:38265, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61189] Another function of VGAM1845 is therefore inhibition of LOC146909 (Accession XM\_085634). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146909. LOC147080 (Accession XM\_097182) is another VGAM1845 host target gene. LOC147080 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147080, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC147080 BINDING SITE, designated SEQ ID:40797, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61190] Another function of VGAM1845 is therefore inhibition of LOC147080 (Accession XM\_097182). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147080. LOC147299 (Accession XM\_085763) is another VGAM1845 host target gene. LOC147299 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147299 BINDING SITE, designated SEQ ID:38329, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61191] Another function of VGAM1845 is therefore inhibition of LOC147299 (Accession XM\_085763). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147299. LOC151701 (Accession XM\_098109) is an-

other VGAM1845 host target gene. LOC151701 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151701, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151701 BINDING SITE, designated SEQ ID:41384, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61192] Another function of VGAM1845 is therefore inhibition of LOC151701 (Accession XM\_098109). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151701. LOC154877 (Accession XM\_098626) is another VGAM1845 host target gene. LOC154877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154877 BINDING SITE, designated SEQ ID:41739, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61193] Another function of VGAM1845 is therefore inhibition of LOC154877 (Accession XM\_098626). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154877. LOC220002 (Accession XM\_166224) is another VGAM1845 host target gene. LOC220002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220002 BINDING SITE, designated SEQ ID:44047, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61194] Another function of VGAM1845 is therefore inhibition of LOC220002 (Accession XM\_166224). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220002. LOC91115 (Accession XM\_036218) is another VGAM1845 host target gene. LOC91115 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91115, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91115 BINDING SITE, designated SEQ ID:32393, to the nucleotide sequence of VGAM1845 RNA, herein designated VGAM RNA, also designated SEQ ID:4556.

[61195] Another function of VGAM1845 is therefore inhibition of LOC91115 (Accession XM\_036218). Accordingly, utilities of VGAM1845 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91115. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1846 (VGAM1846) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61196] VGAM1846 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1846 was detected is described hereinabove with reference to Figs. 1–8.

[61197] VGAM1846 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1846 host target gene, herein desig-

nated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61198] VGAM1846 gene encodes a VGAM1846 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1846 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1846 precursor RNA is designated SEQ ID:1832, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1832 is located at position 16140 relative to the genome of Chimpanzee Cytomegalovirus.

[61199] VGAM1846 precursor RNA folds onto itself, forming VGAM1846 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61200] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1846 folded precursor RNA into VGAM1846

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1846 RNA is designated SEQ ID:4557, and is provided hereinbelow with reference to the sequence listing part.

[61201] VGAM1846 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1846 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1846 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61202] VGAM1846 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1846 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1846 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1846 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1846 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61203] The complementary binding of VGAM1846 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1846 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1846 host target RNA into VGAM1846 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM



host target protein is therefore outlined by a broken line.

[61204] It is appreciated that VGAM1846 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1846 host target genes. The mRNA of each one of this plurality of VGAM1846 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1846 RNA, herein designated VGAM RNA, and which when bound by VGAM1846 RNA causes inhibition of translation of respective one or more VGAM1846 host target proteins.

[61205] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1846 gene, herein designated VGAM GENE, on one or more VGAM1846 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61206] It is yet further appreciated that a function of VGAM1846 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1846 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1846 correlate with, and may be deduced from, the identity of the host target genes which VGAM1846 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61207] Nucleotide sequences of the VGAM1846 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1846 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1846 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1846 are further described hereinbelow with reference to Table 1.

[61208] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1846 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1846 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61209] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1846 gene, herein designated VGAM is inhibition of expression of VGAM1846 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1846 correlate with, and may be deduced from, the identity of the target genes which VGAM1846 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61210] FLJ10713 (Accession NM\_018189) is a VGAM1846 host target gene. FLJ10713 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10713 BINDING SITE, designated SEQ ID:20039, to the nucleotide sequence of VGAM1846 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4557.

[61211] A function of VGAM1846 is therefore inhibition of FLJ10713 (Accession NM\_018189). Accordingly, utilities of VGAM1846 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10713. FLJ22794 (Accession XM\_166220) is another VGAM1846 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44031, to the nucleotide sequence of VGAM1846 RNA, herein designated VGAM RNA, also designated SEQ ID:4557.

[61212] Another function of VGAM1846 is therefore inhibition of FLJ22794 (Accession XM\_166220). Accordingly, utilities of VGAM1846 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. LOC152271 (Accession XM\_087419) is another VGAM1846 host target gene. LOC152271 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152271, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152271 BINDING SITE, designated SEQ ID:39239, to the nucleotide sequence of VGAM1846 RNA, herein designated VGAM RNA, also designated SEQ ID:4557.

[61213] Another function of VGAM1846 is therefore inhibition of LOC152271 (Accession XM\_087419). Accordingly, utilities of VGAM1846 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152271. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1847 (VGAM1847) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61214] VGAM1847 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1847 was detected is described hereinabove with reference to Figs. 1-8.

[61215] VGAM1847 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sonchus Yellow Net

Virus. VGAM1847 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61216] VGAM1847 gene encodes a VGAM1847 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1847 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1847 precursor RNA is designated SEQ ID:1833, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1833 is located at position 6650 relative to the genome of Sonchus Yellow Net Virus.

[61217] VGAM1847 precursor RNA folds onto itself, forming VGAM1847 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61218] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1847 folded precursor RNA into VGAM1847 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1847 RNA is designated SEQ ID:4558, and is provided hereinbelow with reference to the sequence listing part.

[61219] VGAM1847 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1847 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1847 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61220] VGAM1847 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1847 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1847 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1847 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1847 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61221] The complementary binding of VGAM1847 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1847 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1847 host target RNA into VGAM1847 host target protein,



herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61222] It is appreciated that VGAM1847 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1847 host target genes. The mRNA of each one of this plurality of VGAM1847 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1847 RNA, herein designated VGAM RNA, and which when bound by VGAM1847 RNA causes inhibition of translation of respective one or more VGAM1847 host target proteins.

[61223] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1847 gene, herein designated VGAM GENE, on one or more VGAM1847 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61224] It is yet further appreciated that a function of VGAM1847 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1847 include diagnosis, prevention and treatment of viral infection by Sonchus Yellow Net Virus. Specific functions, and accordingly utilities, of VGAM1847 correlate with, and may be deduced from, the identity of the host target genes which VGAM1847 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61225] Nucleotide sequences of the VGAM1847 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1847 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1847 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1847 are further described hereinbelow with reference to Table 1.

[61226] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1847 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1847 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61227] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1847 gene, herein designated VGAM is inhibition of expression of VGAM1847 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1847 correlate with, and may be deduced from, the identity of the target genes which VGAM1847 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61228] Absent In Melanoma 1 (AIM1, Accession XM\_166300) is a VGAM1847 host target gene. AIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AIM1 BINDING SITE, designated SEQ ID:44113, to the nucleotide sequence of

VGAM1847 RNA, herein designated VGAM RNA, also designated SEQ ID:4558.

[61229] A function of VGAM1847 is therefore inhibition of Absent In Melanoma 1 (AIM1, Accession XM\_166300), a gene which interactions with the cytoskeleton. Accordingly, utilities of VGAM1847 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AIM1. The function of AIM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM808. KIAA1301 (Accession XM\_038999) is another VGAM1847 host target gene. KIAA1301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1301 BINDING SITE, designated SEQ ID:32976, to the nucleotide sequence of VGAM1847 RNA, herein designated VGAM RNA, also designated SEQ ID:4558.

[61230] Another function of VGAM1847 is therefore inhibition of KIAA1301 (Accession XM\_038999). Accordingly, utilities of VGAM1847 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1301. LOC157681 (Accession XM\_088363) is another VGAM1847 host target gene. LOC157681 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC157681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157681 BINDING SITE, designated SEQ ID:39644, to the nucleotide sequence of VGAM1847 RNA, herein designated VGAM RNA, also designated SEQ ID:4558.

[61231] Another function of VGAM1847 is therefore inhibition of LOC157681 (Accession XM\_088363). Accordingly, utilities of VGAM1847 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157681. LOC92391 (Accession XM\_044793) is another VGAM1847 host target gene. LOC92391 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC92391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92391 BINDING SITE, designated SEQ ID:34271, to the

nucleotide sequence of VGAM1847 RNA, herein designated VGAM RNA, also designated SEQ ID:4558.

[61232] Another function of VGAM1847 is therefore inhibition of LOC92391 (Accession XM\_044793). Accordingly, utilities of VGAM1847 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92391. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1848 (VGAM1848) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61233] VGAM1848 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1848 was detected is described hereinabove with reference to Figs. 1–8.

[61234] VGAM1848 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sonchus Yellow Net Virus. VGAM1848 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61235] VGAM1848 gene encodes a VGAM1848 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1848 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1848 precursor RNA is designated SEQ ID:1834, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1834 is located at position 9698 relative to the genome of Sonchus Yellow Net Virus.

[61236] VGAM1848 precursor RNA folds onto itself, forming VGAM1848 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61237] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1848 folded precursor RNA into VGAM1848 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1848 RNA is designated SEQ ID:4559, and is provided hereinbelow with reference to the sequence listing part.

[61238] VGAM1848 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1848 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1848 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61239] VGAM1848 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1848 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1848 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding



sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1848 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1848 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61240] The complementary binding of VGAM1848 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1848 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1848 host target RNA into VGAM1848 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61241] It is appreciated that VGAM1848 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1848 host target genes. The mRNA of each one of this plurality of VGAM1848 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1848 RNA, herein designated VGAM RNA, and which when bound by VGAM1848 RNA causes inhibition of translation of respective one or more VGAM1848 host target proteins.

[61242] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1848 gene, herein designated VGAM GENE, on one or more VGAM1848 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[61243] It is yet further appreciated that a function of VGAM1848 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1848 include diagnosis, prevention and treatment of viral infection by Sonchus Yellow Net Virus. Specific functions, and accordingly utilities, of VGAM1848 correlate with, and may be deduced from, the identity of the host target genes which VGAM1848 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61244] Nucleotide sequences of the VGAM1848 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1848 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1848 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1848 are further described hereinbelow with reference to Table 1.

[61245] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1848 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1848 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61246] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1848 gene, herein designated VGAM is inhibition of expression of VGAM1848 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1848 correlate with, and may be deduced from, the identity of the target genes which VGAM1848 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61247] Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 6 (SLC9A6, Accession NM\_006359) is a VGAM1848 host target gene. SLC9A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC9A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC9A6 BINDING SITE, designated SEQ ID:13052, to the nucleotide sequence of VGAM1848 RNA, herein designated VGAM RNA, also designated SEQ ID:4559.

[61248] A function of VGAM1848 is therefore inhibition of Solute

Carrier Family 9 (sodium/hydrogen exchanger), Isoform 6 (SLC9A6, Accession NM\_006359), a gene which is involved electroneutral exchange of protons for  $\text{Na}^+$  and  $\text{K}^+$  across the mitochondrial inner membrane. Accordingly, utilities of VGAM1848 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC9A6. The function of SLC9A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM493.SPF30 (Accession NM\_005871) is another VGAM1848 host target gene. SPF30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPF30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPF30 BINDING SITE, designated SEQ ID:12489, to the nucleotide sequence of VGAM1848 RNA, herein designated VGAM RNA, also designated SEQ ID:4559.

[61249] Another function of VGAM1848 is therefore inhibition of SPF30 (Accession NM\_005871). Accordingly, utilities of VGAM1848 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPF30.

FLJ10035 (Accession NM\_017974) is another VGAM1848 host target gene. FLJ10035 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10035, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10035 BINDING SITE, designated SEQ ID:19706, to the nucleotide sequence of VGAM1848 RNA, herein designated VGAM RNA, also designated SEQ ID:4559.

[61250] Another function of VGAM1848 is therefore inhibition of FLJ10035 (Accession NM\_017974). Accordingly, utilities of VGAM1848 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10035. Pellino Homolog 1 (Drosophila) (PELI1, Accession NM\_020651) is another VGAM1848 host target gene. PELI1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PELI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PELI1 BINDING SITE, designated SEQ ID:21813, to the nucleotide sequence of VGAM1848 RNA, herein

designated VGAM RNA, also designated SEQ ID:4559.

[61251] Another function of VGAM1848 is therefore inhibition of Pellino Homolog 1 (Drosophila) (PELI1, Accession NM\_020651). Accordingly, utilities of VGAM1848 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PELI1. LOC145786 (Accession XM\_096860) is another VGAM1848 host target gene. LOC145786 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145786 BINDING SITE, designated SEQ ID:40590, to the nucleotide sequence of VGAM1848 RNA, herein designated VGAM RNA, also designated SEQ ID:4559.

[61252] Another function of VGAM1848 is therefore inhibition of LOC145786 (Accession XM\_096860). Accordingly, utilities of VGAM1848 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145786. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1849 (VGAM1849) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61253] VGAM1849 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1849 was detected is described hereinabove with reference to Figs. 1–8.

[61254] VGAM1849 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpea Chlorotic Mottle Virus. VGAM1849 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61255] VGAM1849 gene encodes a VGAM1849 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1849 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1849 precursor RNA is designated SEQ ID:1835, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1835 is located at position 1870 relative to the genome of Cowpea Chlorotic Mottle Virus.



[61256] VGAM1849 precursor RNA folds onto itself, forming VGAM1849 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61257] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1849 folded precursor RNA into VGAM1849 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1849 RNA is designated SEQ ID:4560, and is provided hereinbelow with reference to the sequence listing part.

[61258] VGAM1849 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1849 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1849 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61259] VGAM1849 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1849 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1849 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1849 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1849 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61260] The complementary binding of VGAM1849 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1849 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1849 host target RNA into VGAM1849 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61261] It is appreciated that VGAM1849 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1849 host target genes. The mRNA of each one of this plurality of VGAM1849 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1849 RNA, herein designated VGAM RNA, and which when bound by VGAM1849 RNA causes inhibition of translation of respective one or more VGAM1849 host target proteins.

[61262] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1849 gene, herein designated VGAM GENE, on one or more VGAM1849 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61263] It is yet further appreciated that a function of VGAM1849 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of viral infection by Cowpea Chlorotic Mottle Virus. Specific functions, and accordingly utilities, of VGAM1849 correlate with, and may be deduced from, the

identity of the host target genes which VGAM1849 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61264] Nucleotide sequences of the VGAM1849 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1849 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1849 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1849 are further described hereinbelow with reference to Table 1.

[61265] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1849 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1849 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61266] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1849 gene, herein designated VGAM is inhibition of expression of VGAM1849 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1849 correlate with, and may be deduced from, the identity of the target genes which VGAM1849

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61267] ATPase, Class VI, Type 11B (ATP11B, Accession XM\_087254) is a VGAM1849 host target gene. ATP11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP11B BINDING SITE, designated SEQ ID:39147, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61268] A function of VGAM1849 is therefore inhibition of ATPase, Class VI, Type 11B (ATP11B, Accession XM\_087254), a gene which is phosphorylated in their intermediate state, drives uphill transport of ions across membranes. Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP11B. The function of ATP11B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM665. Phosphoinositide-3-kinase, Class 2, Beta

Polypeptide (PIK3C2B, Accession NM\_002646) is another VGAM1849 host target gene. PIK3C2B BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PIK3C2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3C2B BINDING SITE, designated SEQ ID:8505, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61269] Another function of VGAM1849 is therefore inhibition of Phosphoinositide-3-kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM\_002646). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3C2B. Cell Division Cycle Associated 7 (CDCA7, Accession NM\_031942) is another VGAM1849 host target gene. CDCA7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDCA7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDCA7 BINDING SITE, designated SEQ

ID:25687, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61270] Another function of VGAM1849 is therefore inhibition of Cell Division Cycle Associated 7 (CDCA7, Accession NM\_031942). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDCA7. Hyaluronan Binding Protein 2 (HABP2, Accession NM\_004132) is another VGAM1849 host target gene. HABP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HABP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HABP2 BINDING SITE, designated SEQ ID:10342, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61271] Another function of VGAM1849 is therefore inhibition of Hyaluronan Binding Protein 2 (HABP2, Accession NM\_004132). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HABP2. KIAA0523



(Accession XM\_041964) is another VGAM1849 host target gene. KIAA0523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0523 BINDING SITE, designated SEQ ID:33642, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61272] Another function of VGAM1849 is therefore inhibition of KIAA0523 (Accession XM\_041964). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0523. LOC122618 (Accession NM\_138790) is another VGAM1849 host target gene. LOC122618 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC122618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122618 BINDING SITE, designated SEQ ID:29014, to the nucleotide sequence of VGAM1849 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4560.

[61273] Another function of VGAM1849 is therefore inhibition of LOC122618 (Accession NM\_138790). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122618. LOC154739 (Accession XM\_098602) is another VGAM1849 host target gene. LOC154739 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154739 BINDING SITE, designated SEQ ID:41720, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61274] Another function of VGAM1849 is therefore inhibition of LOC154739 (Accession XM\_098602). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154739. LOC203276 (Accession XM\_117523) is another VGAM1849 host target gene. LOC203276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203276, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203276 BINDING SITE, designated SEQ ID:43489, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61275] Another function of VGAM1849 is therefore inhibition of LOC203276 (Accession XM\_117523). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203276. LOC203305 (Accession XM\_117529) is another VGAM1849 host target gene. LOC203305 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203305 BINDING SITE, designated SEQ ID:43513, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61276] Another function of VGAM1849 is therefore inhibition of LOC203305 (Accession XM\_117529). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC203305. LOC204970 (Accession XM\_114795) is another VGAM1849 host target gene. LOC204970 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204970 BINDING SITE, designated SEQ ID:43071, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61277] Another function of VGAM1849 is therefore inhibition of LOC204970 (Accession XM\_114795). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204970. LOC206324 (Accession XM\_121162) is another VGAM1849 host target gene. LOC206324 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC206324, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC206324 BINDING SITE, designated SEQ ID:43612, to

the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61278] Another function of VGAM1849 is therefore inhibition of LOC206324 (Accession XM\_121162). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC206324. LOC219894 (Accession XM\_167782) is another VGAM1849 host target gene. LOC219894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219894 BINDING SITE, designated SEQ ID:44797, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61279] Another function of VGAM1849 is therefore inhibition of LOC219894 (Accession XM\_167782). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219894. LOC254243 (Accession XM\_173233) is another VGAM1849 host target gene. LOC254243 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC254243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254243 BINDING SITE, designated SEQ ID:46515, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61280] Another function of VGAM1849 is therefore inhibition of LOC254243 (Accession XM\_173233). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254243. LOC90038 (Accession XM\_028305) is another VGAM1849 host target gene. LOC90038 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90038 BINDING SITE, designated SEQ ID:30652, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61281] Another function of VGAM1849 is therefore inhibition of LOC90038 (Accession XM\_028305). Accordingly, utilities

of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90038. LOC91796 (Accession XM\_040743) is another VGAM1849 host target gene. LOC91796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91796 BINDING SITE, designated SEQ ID:33373, to the nucleotide sequence of VGAM1849 RNA, herein designated VGAM RNA, also designated SEQ ID:4560.

[61282] Another function of VGAM1849 is therefore inhibition of LOC91796 (Accession XM\_040743). Accordingly, utilities of VGAM1849 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91796. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1850 (VGAM1850) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61283] VGAM1850 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1850 was detected is described hereinabove with reference to Figs. 1–8.

[61284] VGAM1850 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sonchus Yellow Net Virus. VGAM1850 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61285] VGAM1850 gene encodes a VGAM1850 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1850 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1850 precursor RNA is designated SEQ ID:1836, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1836 is located at position 1237 relative to the genome of Sonchus Yellow Net Virus.

[61286] VGAM1850 precursor RNA folds onto itself, forming VGAM1850 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the



art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61287] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1850 folded precursor RNA into VGAM1850 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM1850 RNA is designated SEQ ID:4561, and is provided hereinbelow with reference to the sequence listing part.

[61288] VGAM1850 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1850 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1850 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[61289] VGAM1850 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1850 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1850 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1850 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1850 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61290] The complementary binding of VGAM1850 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1850 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1850 host target RNA into VGAM1850 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61291] It is appreciated that VGAM1850 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1850 host target genes. The mRNA of each one of this plurality of VGAM1850 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1850 RNA, herein designated VGAM RNA, and which when bound by VGAM1850 RNA causes inhibition of translation of respective one or more VGAM1850 host target proteins.

[61292] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1850 gene, herein designated VGAM GENE, on one or more VGAM1850 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61293] It is yet further appreciated that a function of VGAM1850 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1850 include diagnosis, prevention and treatment of viral infection by Sonchus Yellow Net Virus. Specific functions, and accordingly utilities, of VGAM1850 correlate with, and may be deduced from, the identity of the host target genes which VGAM1850 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61294] Nucleotide sequences of the VGAM1850 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1850 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1850 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1850 are further  
described hereinbelow with reference to Table 1.

[61295] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1850 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1850 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[61296] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1850 gene, herein designated VGAM is  
inhibition of expression of VGAM1850 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1850 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1850  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[61297] BCRP2 (Accession XM\_031102) is a VGAM1850 host target  
gene. BCRP2 BINDING SITE is HOST TARGET binding site

found in the 3` untranslated region of mRNA encoded by BCRP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCRP2 BINDING SITE, designated SEQ ID:31276, to the nucleotide sequence of VGAM1850 RNA, herein designated VGAM RNA, also designated SEQ ID:4561.

[61298] A function of VGAM1850 is therefore inhibition of BCRP2 (Accession XM\_031102). Accordingly, utilities of VGAM1850 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCRP2. Neural Cell Adhesion Molecule 2 (NCAM2, Accession NM\_004540) is another VGAM1850 host target gene. NCAM2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NCAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCAM2 BINDING SITE, designated SEQ ID:10891, to the nucleotide sequence of VGAM1850 RNA, herein designated VGAM RNA, also designated SEQ ID:4561.

[61299] Another function of VGAM1850 is therefore inhibition of Neural Cell Adhesion Molecule 2 (NCAM2, Accession NM\_004540). Accordingly, utilities of VGAM1850 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCAM2. Di-Ras2 (Accession NM\_017594) is another VGAM1850 host target gene. Di-Ras2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Di-Ras2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Di-Ras2 BINDING SITE, designated SEQ ID:19045, to the nucleotide sequence of VGAM1850 RNA, herein designated VGAM RNA, also designated SEQ ID:4561.

[61300] Another function of VGAM1850 is therefore inhibition of Di-Ras2 (Accession NM\_017594). Accordingly, utilities of VGAM1850 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Di-Ras2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1851 (VGAM1851) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61301] VGAM1851 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1851 was detected is described hereinabove with reference to Figs. 1–8.

[61302] VGAM1851 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sonchus Yellow Net Virus. VGAM1851 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61303] VGAM1851 gene encodes a VGAM1851 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1851 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1851 precursor RNA is designated SEQ ID:1837, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1837 is located at position 6021 relative to the genome of Sonchus Yellow Net Virus.

[61304] VGAM1851 precursor RNA folds onto itself, forming



VGAM1851 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61305] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1851 folded precursor RNA into VGAM1851 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1851 RNA is designated SEQ ID:4562, and is provided hereinbelow with reference to the sequence listing part.

[61306] VGAM1851 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1851 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1851 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61307] VGAM1851 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1851 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1851 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1851 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1851 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61308] The complementary binding of VGAM1851 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1851 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1851 host target RNA into VGAM1851 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61309] It is appreciated that VGAM1851 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1851 host target genes. The mRNA of each one of this plurality of VGAM1851 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1851 RNA, herein designated VGAM RNA, and which when bound by VGAM1851 RNA causes inhibition of translation of respective one or more VGAM1851 host target proteins.

[61310] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1851 gene, herein designated VGAM GENE, on one or more VGAM1851 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61311] It is yet further appreciated that a function of VGAM1851 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of viral infection by Sonchus Yellow Net Virus. Specific functions, and accordingly utilities, of VGAM1851 correlate with, and may be deduced from, the identity of the host target genes which VGAM1851 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[61312] Nucleotide sequences of the VGAM1851 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1851 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1851 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1851 are further described hereinbelow with reference to Table 1.

[61313] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1851 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1851 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61314] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1851 gene, herein designated VGAM is inhibition of expression of VGAM1851 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1851 correlate with, and may be deduced from, the identity of the target genes which VGAM1851 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[61315] Amyloid Beta Precursor Protein (cytoplasmic tail) Binding Protein 2 (APPBP2, Accession NM\_006380) is a VGAM1851 host target gene. APPBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APPBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APPBP2 BINDING SITE, designated SEQ ID:13079, to the nucleotide sequence of VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.

[61316] A function of VGAM1851 is therefore inhibition of Amyloid Beta Precursor Protein (cytoplasmic tail) Binding Protein 2 (APPBP2, Accession NM\_006380), a gene which interacts with the basolateral sorting signal of amyloid precursor protein. Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APPBP2. The function of APPBP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM525.Lectin, Mannose-binding, 1 (LMAN1, Accession

NM\_005570) is another VGAM1851 host target gene. LMAN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LMAN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMAN1 BINDING SITE, designated SEQ ID:12097, to the nucleotide sequence of VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.

[61317] Another function of VGAM1851 is therefore inhibition of Lectin, Mannose-binding, 1 (LMAN1, Accession NM\_005570). Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMAN1. Ring Finger Protein 14 (RNF14, Accession NM\_004290) is another VGAM1851 host target gene. RNF14 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RNF14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF14 BINDING SITE, designated SEQ ID:10502, to the nucleotide sequence of

VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.

[61318] Another function of VGAM1851 is therefore inhibition of Ring Finger Protein 14 (RNF14, Accession NM\_004290), a gene which associates with the androgen receptor (AR); functions as a transcriptional coactivator. Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF14. The function of RNF14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827. Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM\_114281) is another VGAM1851 host target gene. SCN1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SCN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN1A BINDING SITE, designated SEQ ID:42830, to the nucleotide sequence of VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.



[61319] Another function of VGAM1851 is therefore inhibition of Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM\_114281). Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN1A. FLJ20274 (Accession XM\_031455) is another VGAM1851 host target gene. FLJ20274 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20274 BINDING SITE, designated SEQ ID:31386, to the nucleotide sequence of VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.

[61320] Another function of VGAM1851 is therefore inhibition of FLJ20274 (Accession XM\_031455). Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20274. FLJ21617 (Accession NM\_030897) is another VGAM1851 host target gene. FLJ21617 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21617, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21617 BINDING SITE, designated SEQ ID:25165, to the nucleotide sequence of VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.

[61321] Another function of VGAM1851 is therefore inhibition of FLJ21617 (Accession NM\_030897). Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21617. KATII (Accession NM\_016228) is another VGAM1851 host target gene. KATII BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KATII, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KATII BINDING SITE, designated SEQ ID:18343, to the nucleotide sequence of VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.

[61322] Another function of VGAM1851 is therefore inhibition of KATII (Accession NM\_016228). Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KATII. KIAA0090 (Accession XM\_114045) is another VGAM1851 host target gene. KIAA0090 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0090, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0090 BINDING SITE, designated SEQ ID:42650, to the nucleotide sequence of VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.

[61323] Another function of VGAM1851 is therefore inhibition of KIAA0090 (Accession XM\_114045). Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0090. NYD-SP16 (Accession NM\_031952) is another VGAM1851 host target gene. NYD-SP16 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NYD-SP16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NYD-SP16 BINDING SITE, designated SEQ ID:25693, to the nu-

cleotide sequence of VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.

[61324] Another function of VGAM1851 is therefore inhibition of NYD-SP16 (Accession NM\_031952). Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NYD-SP16. LOC203378 (Accession XM\_117541) is another VGAM1851 host target gene. LOC203378 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203378, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203378 BINDING SITE, designated SEQ ID:43557, to the nucleotide sequence of VGAM1851 RNA, herein designated VGAM RNA, also designated SEQ ID:4562.

[61325] Another function of VGAM1851 is therefore inhibition of LOC203378 (Accession XM\_117541). Accordingly, utilities of VGAM1851 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203378. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1852 (VGAM1852) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61326] VGAM1852 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1852 was detected is described hereinabove with reference to Figs. 1–8.

[61327] VGAM1852 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sonchus Yellow Net Virus. VGAM1852 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61328] VGAM1852 gene encodes a VGAM1852 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1852 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1852 precursor RNA is designated SEQ ID:1838, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1838 is located at position 1792 relative to the genome of Sonchus Yellow Net Virus.

[61329] VGAM1852 precursor RNA folds onto itself, forming VGAM1852 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61330] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1852 folded precursor RNA into VGAM1852 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1852 RNA is designated SEQ ID:4563, and is provided hereinbelow with reference to the sequence listing part.

[61331] VGAM1852 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1852 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1852 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61332] VGAM1852 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1852 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1852 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1852 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1852 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61333] The complementary binding of VGAM1852 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1852 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1852 host target RNA into VGAM1852 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61334] It is appreciated that VGAM1852 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1852 host target genes. The mRNA of each one of this plurality of VGAM1852 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1852 RNA, herein designated VGAM RNA, and which when bound by VGAM1852 RNA causes inhibition of translation of respective one or more VGAM1852 host target proteins.

[61335] It is further appreciated by one skilled in the art that the



mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1852 gene, herein designated VGAM GENE, on one or more VGAM1852 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61336] It is yet further appreciated that a function of VGAM1852 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1852 include diagnosis, prevention and treatment of viral infection by Sonchus Yellow Net Virus. Specific functions, and accordingly utilities, of VGAM1852 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1852 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61337] Nucleotide sequences of the VGAM1852 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1852 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1852 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1852 are further described hereinbelow with reference to Table 1.

[61338] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1852 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1852 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61339] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1852 gene, herein designated VGAM is inhibition of expression of VGAM1852 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1852 correlate with, and may be deduced from, the identity of the target genes which VGAM1852

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61340] ATP-binding Cassette, Sub-family B (MDR/TAP), Member 4 (ABCB4, Accession NM\_000443) is a VGAM1852 host target gene. ABCB4 BINDING SITE1 and ABCB4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABCB4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCB4 BINDING SITE1 and ABCB4 BINDING SITE2, designated SEQ ID:6029 and SEQ ID:20834 respectively, to the nucleotide sequence of VGAM1852 RNA, herein designated VGAM RNA, also designated SEQ ID:4563.

[61341] A function of VGAM1852 is therefore inhibition of ATP-binding Cassette, Sub-family B (MDR/TAP), Member 4 (ABCB4, Accession NM\_000443). Accordingly, utilities of VGAM1852 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCB4. 5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868) is another VGAM1852 host target gene. HTR2C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

HTR2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR2C BINDING SITE, designated SEQ ID:6532, to the nucleotide sequence of VGAM1852 RNA, herein designated VGAM RNA, also designated SEQ ID:4563.

[61342] Another function of VGAM1852 is therefore inhibition of 5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868), a gene which activates phospholipase C and regulates intracellular calcium flux. Accordingly, utilities of VGAM1852 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR2C. The function of HTR2C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1052. CGG Triplet Repeat Binding Protein 1 (CGGBP1, Accession NM\_003663) is another VGAM1852 host target gene. CGGBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGGBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of CGGBP1 BINDING SITE, designated SEQ ID:9743, to the nucleotide sequence of VGAM1852 RNA, herein designated VGAM RNA, also designated SEQ ID:4563.

[61343] Another function of VGAM1852 is therefore inhibition of CGG Triplet Repeat Binding Protein 1 (CGGBP1, Accession NM\_003663). Accordingly, utilities of VGAM1852 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGGBP1. DKFZP434G1411 (Accession XM\_166383) is another VGAM1852 host target gene. DKFZP434G1411 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434G1411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434G1411 BINDING SITE, designated SEQ ID:44231, to the nucleotide sequence of VGAM1852 RNA, herein designated VGAM RNA, also designated SEQ ID:4563.

[61344] Another function of VGAM1852 is therefore inhibition of DKFZP434G1411 (Accession XM\_166383). Accordingly, utilities of VGAM1852 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZP434G1411. FLJ10154 (Accession NM\_018011) is another VGAM1852 host target gene. FLJ10154 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10154 BINDING SITE, designated SEQ ID:19744, to the nucleotide sequence of VGAM1852 RNA, herein designated VGAM RNA, also designated SEQ ID:4563.

[61345] Another function of VGAM1852 is therefore inhibition of FLJ10154 (Accession NM\_018011). Accordingly, utilities of VGAM1852 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10154. FLJ14281 (Accession NM\_024920) is another VGAM1852 host target gene. FLJ14281 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14281 BINDING SITE, designated SEQ ID:24451, to the nucleotide sequence of VGAM1852 RNA, herein designated VGAM

RNA, also designated SEQ ID:4563.

[61346] Another function of VGAM1852 is therefore inhibition of FLJ14281 (Accession NM\_024920). Accordingly, utilities of VGAM1852 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14281. FLJ20457 (Accession NM\_017832) is another VGAM1852 host target gene. FLJ20457 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20457, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20457 BINDING SITE, designated SEQ ID:19497, to the nucleotide sequence of VGAM1852 RNA, herein designated VGAM RNA, also designated SEQ ID:4563.

[61347] Another function of VGAM1852 is therefore inhibition of FLJ20457 (Accession NM\_017832). Accordingly, utilities of VGAM1852 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20457. Glia Maturation Factor, Beta (GMFB, Accession NM\_004124) is another VGAM1852 host target gene. GMFB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GMFB,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GMFB BINDING SITE, designated SEQ ID:10327, to the nucleotide sequence of VGAM1852 RNA, herein designated VGAM RNA, also designated SEQ ID:4563.

[61348] Another function of VGAM1852 is therefore inhibition of Glia Maturation Factor, Beta (GMFB, Accession NM\_004124). Accordingly, utilities of VGAM1852 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMFB. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1853 (VGAM1853) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61349] VGAM1853 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1853 was detected is described hereinabove with reference to Figs. 1–8.

[61350] VGAM1853 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sonchus Yellow Net



Virus. VGAM1853 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61351] VGAM1853 gene encodes a VGAM1853 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1853 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1853 precursor RNA is designated SEQ ID:1839, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1839 is located at position 3373 relative to the genome of Sonchus Yellow Net Virus.

[61352] VGAM1853 precursor RNA folds onto itself, forming VGAM1853 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61353] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1853 folded precursor RNA into VGAM1853 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1853 RNA is designated SEQ ID:4564, and is provided hereinbelow with reference to the sequence listing part.

[61354] VGAM1853 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1853 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1853 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61355] VGAM1853 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1853 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1853 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1853 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1853 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61356] The complementary binding of VGAM1853 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1853 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1853 host target RNA into VGAM1853 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61357] It is appreciated that VGAM1853 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1853 host target genes. The mRNA of each one of this plurality of VGAM1853 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1853 RNA, herein designated VGAM RNA, and which when bound by VGAM1853 RNA causes inhibition of translation of respective one or more VGAM1853 host target proteins.

[61358] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1853 gene, herein designated VGAM GENE, on one or more VGAM1853 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61359] It is yet further appreciated that a function of VGAM1853 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of viral infection by Sonchus Yellow Net Virus. Specific functions, and accordingly utilities, of VGAM1853 correlate with, and may be deduced from, the identity of the host target genes which VGAM1853 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61360] Nucleotide sequences of the VGAM1853 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1853 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1853 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1853 are further described hereinbelow with reference to Table 1.

[61361] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1853 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1853 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61362] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1853 gene, herein designated VGAM is inhibition of expression of VGAM1853 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1853 correlate with, and may be deduced from, the identity of the target genes which VGAM1853 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61363] Cadherin 17, LI Cadherin (liver-intestine) (CDH17, Accession NM\_004063) is a VGAM1853 host target gene. CDH17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH17 BINDING SITE, designated SEQ

ID:10270, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61364] A function of VGAM1853 is therefore inhibition of Cadherin 17, LI Cadherin (liver–intestine) (CDH17, Accession NM\_004063), a gene which may have a role in the morphological organization of liver and intestine and involved in intestinal peptide transport. Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH17. The function of CDH17 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM795. Copine III (CPNE3, Accession NM\_003909) is another VGAM1853 host target gene. CPNE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPNE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPNE3 BINDING SITE, designated SEQ ID:9995, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61365] Another function of VGAM1853 is therefore inhibition of Copine III (CPNE3, Accession NM\_003909), a gene which may function in membrane trafficking. Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPNE3. The function of CPNE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. Cullin 3 (CUL3, Accession NM\_003590) is another VGAM1853 host target gene. CUL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CUL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CUL3 BINDING SITE, designated SEQ ID:9646, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61366] Another function of VGAM1853 is therefore inhibition of Cullin 3 (CUL3, Accession NM\_003590), a gene which may target other proteins for ubiquitin-dependent proteolysis. Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical condi-



tions associated with CUL3. The function of CUL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM143. Follistatin-like 1 (FSTL1, Accession NM\_007085) is another VGAM1853 host target gene. FSTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FSTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FSTL1 BINDING SITE, designated SEQ ID:13953, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61367] Another function of VGAM1853 is therefore inhibition of Follistatin-like 1 (FSTL1, Accession NM\_007085), a gene which may modulate the action of some growth factors on cell proliferation and differentiation. Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FSTL1. The function of FSTL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with refer-

ence to VGAM791. Glycoprotein M6A (GPM6A, Accession NM\_005277) is another VGAM1853 host target gene. GPM6A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPM6A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPM6A BINDING SITE, designated SEQ ID:11779, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61368] Another function of VGAM1853 is therefore inhibition of Glycoprotein M6A (GPM6A, Accession NM\_005277), a gene which may play a role in neuronal development. Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPM6A. The function of GPM6A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM326. Interleukin 8 (IL8, Accession XM\_170504) is another VGAM1853 host target gene. IL8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

IL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL8 BINDING SITE, designated SEQ ID:45339, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61369] Another function of VGAM1853 is therefore inhibition of Interleukin 8 (IL8, Accession XM\_170504). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL8. Uridine Monophosphate Synthetase (orotate phosphoribosyl transferase and orotidine-5'-decarboxylase) (UMPS, Accession NM\_000373) is another VGAM1853 host target gene. UMPS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UMPS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UMPS BINDING SITE, designated SEQ ID:5941, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61370] Another function of VGAM1853 is therefore inhibition of

Uridine Monophosphate Synthetase (orotate phosphoribosyl transferase and orotidine-5'-decarboxylase) (UMPS, Accession NM\_000373). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UMPS. Claudin 1 (CLDN1, Accession NM\_021101) is another VGAM1853 host target gene. CLDN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLDN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLDN1 BINDING SITE, designated SEQ ID:22084, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61371] Another function of VGAM1853 is therefore inhibition of Claudin 1 (CLDN1, Accession NM\_021101). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLDN1. DKFZp434E2220 (Accession NM\_017612) is another VGAM1853 host target gene. DKFZp434E2220 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DK-

FZp434E2220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434E2220 BINDING SITE, designated SEQ ID:19112, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61372] Another function of VGAM1853 is therefore inhibition of DKFZp434E2220 (Accession NM\_017612). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434E2220. FLJ12409 (Accession NM\_025105) is another VGAM1853 host target gene. FLJ12409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12409 BINDING SITE, designated SEQ ID:24755, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61373] Another function of VGAM1853 is therefore inhibition of FLJ12409 (Accession NM\_025105). Accordingly, utilities of

VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12409. FLJ20274 (Accession XM\_031455) is another VGAM1853 host target gene. FLJ20274 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20274 BINDING SITE, designated SEQ ID:31387, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61374] Another function of VGAM1853 is therefore inhibition of FLJ20274 (Accession XM\_031455). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20274. FLJ22056 (Accession NM\_022489) is another VGAM1853 host target gene. FLJ22056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22056

BINDING SITE, designated SEQ ID:22870, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61375] Another function of VGAM1853 is therefore inhibition of FLJ22056 (Accession NM\_022489). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22056. FLJ23598 (Accession NM\_024783) is another VGAM1853 host target gene. FLJ23598 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23598 BINDING SITE, designated SEQ ID:24156, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61376] Another function of VGAM1853 is therefore inhibition of FLJ23598 (Accession NM\_024783). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23598. HIC (Accession XM\_041273) is another VGAM1853 host target gene. HIC BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by HIC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC BINDING SITE, designated SEQ ID:33493, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61377] Another function of VGAM1853 is therefore inhibition of HIC (Accession XM\_041273). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC. KIAA1500 (Accession XM\_034353) is another VGAM1853 host target gene. KIAA1500 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1500, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1500 BINDING SITE, designated SEQ ID:32068, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61378] Another function of VGAM1853 is therefore inhibition of



KIAA1500 (Accession XM\_034353). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1500. Myosin, Heavy Polypeptide 10, Non-muscle (MYH10, Accession XM\_044702) is another VGAM1853 host target gene. MYH10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYH10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYH10 BINDING SITE, designated SEQ ID:34266, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61379] Another function of VGAM1853 is therefore inhibition of Myosin, Heavy Polypeptide 10, Non-muscle (MYH10, Accession XM\_044702). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYH10. PRO0082 (Accession NM\_018590) is another VGAM1853 host target gene. PRO0082 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0082, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0082 BINDING SITE, designated SEQ ID:20670, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61380] Another function of VGAM1853 is therefore inhibition of PRO0082 (Accession NM\_018590). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0082. Solute Carrier Family 6 (neurotransmitter transporter), Member 14 (SLC6A14, Accession NM\_007231) is another VGAM1853 host target gene. SLC6A14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A14 BINDING SITE, designated SEQ ID:14102, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61381] Another function of VGAM1853 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter),

Member 14 (SLC6A14, Accession NM\_007231). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A14. LOC256733 (Accession XM\_173116) is another VGAM1853 host target gene. LOC256733 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256733, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256733 BINDING SITE, designated SEQ ID:46369, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61382] Another function of VGAM1853 is therefore inhibition of LOC256733 (Accession XM\_173116). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256733. LOC83690 (Accession NM\_031461) is another VGAM1853 host target gene. LOC83690 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC83690, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC83690 BINDING SITE, designated SEQ ID:25484, to the nucleotide sequence of VGAM1853 RNA, herein designated VGAM RNA, also designated SEQ ID:4564.

[61383] Another function of VGAM1853 is therefore inhibition of LOC83690 (Accession NM\_031461). Accordingly, utilities of VGAM1853 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC83690. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1854 (VGAM1854) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61384] VGAM1854 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1854 was detected is described hereinabove with reference to Figs. 1–8.

[61385] VGAM1854 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpea Chlorotic Mottle Virus. VGAM1854 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61386] VGAM1854 gene encodes a VGAM1854 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1854 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1854 precursor RNA is designated SEQ ID:1840, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1840 is located at position 1253 relative to the genome of Cowpea Chlorotic Mottle Virus.

[61387] VGAM1854 precursor RNA folds onto itself, forming VGAM1854 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61388] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1854 folded precursor RNA into VGAM1854

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1854 RNA is designated SEQ ID:4565, and is provided hereinbelow with reference to the sequence listing part.

[61389] VGAM1854 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1854 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1854 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61390] VGAM1854 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1854 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1854 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1854 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1854 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61391] The complementary binding of VGAM1854 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1854 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1854 host target RNA into VGAM1854 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[61392] It is appreciated that VGAM1854 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1854 host target genes. The mRNA of each one of this plurality of VGAM1854 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1854 RNA, herein designated VGAM RNA, and which when bound by VGAM1854 RNA causes inhibition of translation of respective one or more VGAM1854 host target proteins.

[61393] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1854 gene, herein designated VGAM GENE, on one or more VGAM1854 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61394] It is yet further appreciated that a function of VGAM1854 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1854 include diagnosis, prevention and treatment of viral infection by Cowpea Chlorotic Mottle Virus. Specific functions, and accordingly utilities, of VGAM1854 correlate with, and may be deduced from, the identity of the host target genes which VGAM1854 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61395] Nucleotide sequences of the VGAM1854 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1854 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1854 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1854 are further described hereinbelow with reference to Table 1.

[61396] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1854 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1854 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61397] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1854 gene, herein designated VGAM is inhibition of expression of VGAM1854 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1854 correlate with, and may be deduced from, the identity of the target genes which VGAM1854 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61398] TEA Domain Family Member 3 (TEAD3, Accession NM\_003214) is a VGAM1854 host target gene. TEAD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEAD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEAD3 BINDING SITE, designated SEQ ID:9214, to the nucleotide sequence of VGAM1854 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4565.

[61399] A function of VGAM1854 is therefore inhibition of TEA Domain Family Member 3 (TEAD3, Accession NM\_003214), a gene which binds to multiple functional elements of the human chorionic somatomammotropin- $\beta$  gene enhancer. Accordingly, utilities of VGAM1854 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEAD3. The function of TEAD3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM299.FLJ14442 (Accession NM\_032785) is another VGAM1854 host target gene. FLJ14442 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14442 BINDING SITE, designated SEQ ID:26535, to the nucleotide sequence of VGAM1854 RNA, herein designated VGAM RNA, also designated SEQ ID:4565.

[61400] Another function of VGAM1854 is therefore inhibition of FLJ14442 (Accession NM\_032785). Accordingly, utilities of

VGAM1854 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14442. LOC150998 (Accession XM\_097990) is another VGAM1854 host target gene. LOC150998 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150998, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150998 BINDING SITE, designated SEQ ID:41286, to the nucleotide sequence of VGAM1854 RNA, herein designated VGAM RNA, also designated SEQ ID:4565.

[61401] Another function of VGAM1854 is therefore inhibition of LOC150998 (Accession XM\_097990). Accordingly, utilities of VGAM1854 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150998. LOC256096 (Accession XM\_173164) is another VGAM1854 host target gene. LOC256096 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC256096 BINDING SITE, designated SEQ ID:46419, to the nucleotide sequence of VGAM1854 RNA, herein designated VGAM RNA, also designated SEQ ID:4565.

[61402] Another function of VGAM1854 is therefore inhibition of LOC256096 (Accession XM\_173164). Accordingly, utilities of VGAM1854 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256096. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1855 (VGAM1855) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61403] VGAM1855 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1855 was detected is described hereinabove with reference to Figs. 1–8.

[61404] VGAM1855 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sonchus Yellow Net Virus. VGAM1855 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61405] VGAM1855 gene encodes a VGAM1855 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1855 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1855 precursor RNA is designated SEQ ID:1841, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1841 is located at position 8120 relative to the genome of Sonchus Yellow Net Virus.

[61406] VGAM1855 precursor RNA folds onto itself, forming VGAM1855 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61407] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1855 folded precursor RNA into VGAM1855 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1855 RNA is designated SEQ ID:4566, and is provided hereinbelow with reference to the sequence listing part.

[61408] VGAM1855 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1855 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1855 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61409] VGAM1855 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1855 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1855 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1855 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1855 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61410] The complementary binding of VGAM1855 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1855 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1855 host target RNA into VGAM1855 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61411] It is appreciated that VGAM1855 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1855 host target genes. The mRNA of each one of this plurality of VGAM1855 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1855 RNA, herein designated VGAM RNA, and which when bound by VGAM1855 RNA causes inhibition of translation of respective one or more VGAM1855 host target proteins.

[61412] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1855 gene, herein designated VGAM GENE, on one or more VGAM1855 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[61413] It is yet further appreciated that a function of VGAM1855 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1855 include diagnosis, prevention and treatment of viral infection by Sonchus Yellow Net Virus. Specific functions, and accordingly utilities, of VGAM1855 correlate with, and may be deduced from, the identity of the host target genes which VGAM1855 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61414] Nucleotide sequences of the VGAM1855 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1855 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1855 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1855 are further described hereinbelow with reference to Table 1.

[61415] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1855 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1855 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61416] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1855 gene, herein designated VGAM is inhibition of expression of VGAM1855 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1855 correlate with, and may be deduced from, the identity of the target genes which VGAM1855 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61417] Collagen, Type XV, Alpha 1 (COL15A1, Accession NM\_001855) is a VGAM1855 host target gene. COL15A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL15A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL15A1 BINDING SITE, designated SEQ ID:7587, to the nucleotide sequence of VGAM1855 RNA, herein designated VGAM RNA, also designated SEQ ID:4566.

[61418] A function of VGAM1855 is therefore inhibition of Collagen, Type XV, Alpha 1 (COL15A1, Accession NM\_001855), a gene which may be involved in maintaining the structure of connective tissue. Accordingly, utilities of VGAM1855 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL15A1. The function of COL15A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM304. Myosin IC (MYO1C, Accession XM\_028385) is another VGAM1855 host target gene. MYO1C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYO1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO1C BINDING SITE, designated SEQ ID:30697, to the nucleotide sequence of VGAM1855 RNA, herein designated VGAM RNA, also designated SEQ ID:4566.

[61419] Another function of VGAM1855 is therefore inhibition of Myosin IC (MYO1C, Accession XM\_028385), a gene which participates in adaptation in hair cells. Accordingly, utilities of VGAM1855 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with MYO1C. The function of MYO1C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381.DKFZp564I1922 (Accession NM\_015419) is another VGAM1855 host target gene. DKFZp564I1922 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp564I1922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp564I1922 BINDING SITE, designated SEQ ID:17721, to the nucleotide sequence of VGAM1855 RNA, herein designated VGAM RNA, also designated SEQ ID:4566.

[61420] Another function of VGAM1855 is therefore inhibition of DKFZp564I1922 (Accession NM\_015419). Accordingly, utilities of VGAM1855 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp564I1922. KIAA1579 (Accession NM\_018211) is another VGAM1855 host target gene. KIAA1579 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1579, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1579 BINDING SITE, designated SEQ ID:20116, to the nucleotide sequence of VGAM1855 RNA, herein designated VGAM RNA, also designated SEQ ID:4566.

[61421] Another function of VGAM1855 is therefore inhibition of KIAA1579 (Accession NM\_018211). Accordingly, utilities of VGAM1855 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1579. LOC219686 (Accession XM\_165544) is another VGAM1855 host target gene. LOC219686 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219686, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219686 BINDING SITE, designated SEQ ID:43671, to the nucleotide sequence of VGAM1855 RNA, herein designated VGAM RNA, also designated SEQ ID:4566.

[61422] Another function of VGAM1855 is therefore inhibition of LOC219686 (Accession XM\_165544). Accordingly, utilities of VGAM1855 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC219686. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1856 (VGAM1856) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61423] VGAM1856 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1856 was detected is described hereinabove with reference to Figs. 1–8.

[61424] VGAM1856 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rice Yellow Stunt Virus. VGAM1856 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61425] VGAM1856 gene encodes a VGAM1856 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1856 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1856 precursor RNA is desig-

nated SEQ ID:1842, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1842 is located at position 13503 relative to the genome of Rice Yellow Stunt Virus.

- [61426] VGAM1856 precursor RNA folds onto itself, forming VGAM1856 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [61427] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1856 folded precursor RNA into VGAM1856 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1856 RNA is designated SEQ ID:4567, and is provided hereinbelow with reference to the sequence



listing part.

[61428] VGAM1856 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1856 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1856 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61429] VGAM1856 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1856 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1856 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1856 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1856 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[61430] The complementary binding of VGAM1856 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1856 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1856 host target RNA into VGAM1856 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61431] It is appreciated that VGAM1856 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1856 host target genes. The mRNA of each one of this plurality of VGAM1856 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1856 RNA, herein designated VGAM

RNA, and which when bound by VGAM1856 RNA causes inhibition of translation of respective one or more VGAM1856 host target proteins.

[61432] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1856 gene, herein designated VGAM GENE, on one or more VGAM1856 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61433] It is yet further appreciated that a function of VGAM1856 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1856 include diagnosis, prevention and treatment of viral infection by Rice Yellow Stunt Virus. Specific functions, and accordingly utilities, of VGAM1856 correlate with, and may be deduced from, the identity of the host target genes which VGAM1856 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61434] Nucleotide sequences of the VGAM1856 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1856 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1856 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1856 are further described hereinbelow with reference to Table 1.

[61435] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1856 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1856 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61436] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1856 gene, herein designated VGAM is

inhibition of expression of VGAM1856 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1856 correlate with, and may be deduced from, the identity of the target genes which VGAM1856 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61437] UC28 (Accession NM\_021635) is a VGAM1856 host target gene. UC28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UC28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UC28 BINDING SITE, designated SEQ ID:22279, to the nucleotide sequence of VGAM1856 RNA, herein designated VGAM RNA, also designated SEQ ID:4567.

[61438] A function of VGAM1856 is therefore inhibition of UC28 (Accession NM\_021635). Accordingly, utilities of VGAM1856 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UC28. KIAA1463 (Accession XM\_051160) is another VGAM1856 host target gene. KIAA1463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1463, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1463 BINDING SITE, designated SEQ ID:35770, to the nucleotide sequence of VGAM1856 RNA, herein designated VGAM RNA, also designated SEQ ID:4567.

[61439] Another function of VGAM1856 is therefore inhibition of KIAA1463 (Accession XM\_051160). Accordingly, utilities of VGAM1856 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1463. OBTP (Accession NM\_017601) is another VGAM1856 host target gene. OBTP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OBTP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OBTP BINDING SITE, designated SEQ ID:19077, to the nucleotide sequence of VGAM1856 RNA, herein designated VGAM RNA, also designated SEQ ID:4567.

[61440] Another function of VGAM1856 is therefore inhibition of OBTP (Accession NM\_017601). Accordingly, utilities of VGAM1856 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with OBTP. Protocadherin 20 (PCDH20, Accession NM\_022843) is another VGAM1856 host target gene. PCDH20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH20 BINDING SITE, designated SEQ ID:23135, to the nucleotide sequence of VGAM1856 RNA, herein designated VGAM RNA, also designated SEQ ID:4567.

[61441] Another function of VGAM1856 is therefore inhibition of Protocadherin 20 (PCDH20, Accession NM\_022843). Accordingly, utilities of VGAM1856 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH20. LOC153020 (Accession XM\_087578) is another VGAM1856 host target gene. LOC153020 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153020 BINDING SITE, desig-

nated SEQ ID:39353, to the nucleotide sequence of VGAM1856 RNA, herein designated VGAM RNA, also designated SEQ ID:4567.

[61442] Another function of VGAM1856 is therefore inhibition of LOC153020 (Accession XM\_087578). Accordingly, utilities of VGAM1856 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153020. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1857 (VGAM1857) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61443] VGAM1857 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1857 was detected is described hereinabove with reference to Figs. 1–8.

[61444] VGAM1857 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rice Yellow Stunt Virus. VGAM1857 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.



[61445] VGAM1857 gene encodes a VGAM1857 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1857 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1857 precursor RNA is designated SEQ ID:1843, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1843 is located at position 9634 relative to the genome of Rice Yellow Stunt Virus.

[61446] VGAM1857 precursor RNA folds onto itself, forming VGAM1857 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61447] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1857 folded precursor RNA into VGAM1857 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1857 RNA is designated SEQ ID:4568, and is provided hereinbelow with reference to the sequence listing part.

[61448] VGAM1857 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1857 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1857 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61449] VGAM1857 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1857 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1857 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1857 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1857 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61450] The complementary binding of VGAM1857 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1857 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1857 host target RNA into VGAM1857 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61451] It is appreciated that VGAM1857 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1857 host target genes. The mRNA of each one of this plurality of VGAM1857 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1857 RNA, herein designated VGAM RNA, and which when bound by VGAM1857 RNA causes inhibition of translation of respective one or more VGAM1857 host target proteins.

[61452] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1857 gene, herein designated VGAM GENE, on one or more VGAM1857 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[61453] It is yet further appreciated that a function of VGAM1857 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1857 include diagnosis, prevention and treatment of viral infection by Rice Yellow Stunt Virus. Specific functions, and accordingly utilities, of VGAM1857 correlate with, and may be deduced from, the identity of the host target genes which VGAM1857 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61454] Nucleotide sequences of the VGAM1857 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1857 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1857 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1857 are further described hereinbelow with reference to Table 1.

[61455] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1857 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1857 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61456] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1857 gene, herein designated VGAM is inhibition of expression of VGAM1857 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1857 correlate with, and may be deduced from, the identity of the target genes which VGAM1857 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61457] Alcohol Dehydrogenase IB (class I), Beta Polypeptide (ADH1B, Accession XM\_052365) is a VGAM1857 host target gene. ADH1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADH1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADH1B BINDING SITE, designated SEQ ID:35961, to the nucleotide sequence of VGAM1857 RNA, herein designated VGAM RNA, also designated SEQ ID:4568.

[61458] A function of VGAM1857 is therefore inhibition of Alcohol Dehydrogenase IB (class I), Beta Polypeptide (ADH1B, Accession XM\_052365), a gene which Alcohol dehydrogenase 2 (alcohol:NAD<sup>+</sup> oxidoreductase) class I beta subunit. Accordingly, utilities of VGAM1857 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADH1B. The function of ADH1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1805.Secretory Carrier Membrane Protein 1 (SCAMP1, Accession NM\_004866) is another VGAM1857 host target gene. SCAMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCAMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAMP1 BINDING SITE, designated SEQ ID:11290, to the nucleotide sequence of VGAM1857 RNA, herein designated VGAM RNA, also designated SEQ ID:4568.

[61459] Another function of VGAM1857 is therefore inhibition of Secretory Carrier Membrane Protein 1 (SCAMP1, Accession

NM\_004866), a gene which functions in post-golgi recycling pathways and acts as a recycling carrier to the cell surface. Accordingly, utilities of VGAM1857 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCAMP1. The function of SCAMP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM366. Solute Carrier Family 10 (sodium/bile acid cotransporter family), Member 2 (SLC10A2, Accession NM\_000452) is another VGAM1857 host target gene. SLC10A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC10A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC10A2 BINDING SITE, designated SEQ ID:6063, to the nucleotide sequence of VGAM1857 RNA, herein designated VGAM RNA, also designated SEQ ID:4568.

[61460] Another function of VGAM1857 is therefore inhibition of Solute Carrier Family 10 (sodium/bile acid cotransporter family), Member 2 (SLC10A2, Accession NM\_000452). Ac-



cordingly, utilities of VGAM1857 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC10A2. FLJ20457 (Accession NM\_017832) is another VGAM1857 host target gene. FLJ20457 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20457, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20457 BINDING SITE, designated SEQ ID:19496, to the nucleotide sequence of VGAM1857 RNA, herein designated VGAM RNA, also designated SEQ ID:4568.

[61461] Another function of VGAM1857 is therefore inhibition of FLJ20457 (Accession NM\_017832). Accordingly, utilities of VGAM1857 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20457. KIAA1223 (Accession XM\_048747) is another VGAM1857 host target gene. KIAA1223 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1223, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1223 BINDING SITE, designated SEQ ID:35247, to the nucleotide sequence of VGAM1857 RNA, herein designated VGAM RNA, also designated SEQ ID:4568.

[61462] Another function of VGAM1857 is therefore inhibition of KIAA1223 (Accession XM\_048747). Accordingly, utilities of VGAM1857 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1223. YME1-like 1 (*S. cerevisiae*) (YME1L1, Accession NM\_139312) is another VGAM1857 host target gene. YME1L1 BINDING SITE1 and YME1L1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by YME1L1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YME1L1 BINDING SITE1 and YME1L1 BINDING SITE2, designated SEQ ID:29294 and SEQ ID:15538 respectively, to the nucleotide sequence of VGAM1857 RNA, herein designated VGAM RNA, also designated SEQ ID:4568.

[61463] Another function of VGAM1857 is therefore inhibition of YME1-like 1 (*S. cerevisiae*) (YME1L1, Accession NM\_139312). Accordingly, utilities of VGAM1857 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with YME1L1. LOC256925 (Accession XM\_175065) is another VGAM1857 host target gene. LOC256925 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256925 BINDING SITE, designated SEQ ID:46611, to the nucleotide sequence of VGAM1857 RNA, herein designated VGAM RNA, also designated SEQ ID:4568.

[61464] Another function of VGAM1857 is therefore inhibition of LOC256925 (Accession XM\_175065). Accordingly, utilities of VGAM1857 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256925. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1858 (VGAM1858) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61465] VGAM1858 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1858 was detected is described hereinabove with reference to Figs. 1–8.

[61466] VGAM1858 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rice Yellow Stunt Virus. VGAM1858 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61467] VGAM1858 gene encodes a VGAM1858 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1858 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1858 precursor RNA is designated SEQ ID:1844, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1844 is located at position 4741 relative to the genome of Rice Yellow Stunt Virus.

[61468] VGAM1858 precursor RNA folds onto itself, forming VGAM1858 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61469] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1858 folded precursor RNA into VGAM1858 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1858 RNA is designated SEQ ID:4569, and is provided hereinbelow with reference to the sequence listing part.

[61470] VGAM1858 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1858 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1858 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[61471] VGAM1858 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1858 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1858 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1858 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1858 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61472] The complementary binding of VGAM1858 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1858 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1858 host target RNA into VGAM1858 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61473] It is appreciated that VGAM1858 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1858 host target genes. The mRNA of each one of this plurality of VGAM1858 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1858 RNA, herein designated VGAM RNA, and which when bound by VGAM1858 RNA causes inhibition of translation of respective one or more VGAM1858 host target proteins.

[61474] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1858 gene, herein designated VGAM GENE, on one or more VGAM1858 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61475] It is yet further appreciated that a function of VGAM1858 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of viral infection by Rice Yellow Stunt Virus. Specific functions, and accordingly utilities, of VGAM1858 correlate with, and may be deduced from, the identity of the host target genes which VGAM1858 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61476] Nucleotide sequences of the VGAM1858 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1858 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1858 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1858 are further  
described hereinbelow with reference to Table 1.

[61477] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1858 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1858 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[61478] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1858 gene, herein designated VGAM is  
inhibition of expression of VGAM1858 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1858 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1858  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[61479] Glucosaminyl (N-acetyl) Transferase 2, I-branching En-  
zyme (GCNT2, Accession NM\_001491) is a VGAM1858

host target gene. GCNT2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GCNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCNT2 BINDING SITE, designated SEQ ID:7239, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61480] A function of VGAM1858 is therefore inhibition of Glucosaminyl (N-acetyl) Transferase 2, I-branching Enzyme (GCNT2, Accession NM\_001491), a gene which converts linear into branched poly-n-acetyllactosaminoglycans. Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCNT2. The function of GCNT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM943. Lactate Dehydrogenase B (LDHB, Accession NM\_002300) is another VGAM1858 host target gene. LDHB BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LDHB, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDHB BINDING SITE, designated SEQ ID:8091, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61481] Another function of VGAM1858 is therefore inhibition of Lactate Dehydrogenase B (LDHB, Accession NM\_002300), a gene which causes dehydrogenation of lactate. Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDHB. The function of LDHB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM273. Aminopeptidase Puromycin Sensitive (NPEPPS, Accession NM\_006310) is another VGAM1858 host target gene. NPEPPS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPEPPS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPEPPS BINDING SITE, designated SEQ ID:12998, to the nucleotide se-

quence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61482] Another function of VGAM1858 is therefore inhibition of Aminopeptidase Puromycin Sensitive (NPEPPS, Accession NM\_006310), a gene which is puromycin-sensitive aminopeptidase and has metallopeptidase activity. Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPEPPS. The function of NPEPPS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM83. Protein Tyrosine Phosphatase, Receptor Type, K (PTPRK, Accession NM\_002844) is another VGAM1858 host target gene. PTPRK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPRK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRK BINDING SITE, designated SEQ ID:8733, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61483] Another function of VGAM1858 is therefore inhibition of

Protein Tyrosine Phosphatase, Receptor Type, K (PTPRK, Accession NM\_002844), a gene which regulates of processes involving cell contact and adhesion. Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRK. The function of PTPRK has been established by previous studies. For general information about receptor-type protein-tyrosine phosphatases (PTPs), see PTPRA (OMIM Ref. No. 176884). Yang et al. (1997) used degenerate PCR to identify novel receptor PTPs in a human keratinocyte cDNA library. One of the genes identified was the human homolog of mouse PTPR-kappa. Human PTPR-kappa encodes a 1,440-amino acid polypeptide that is 98% identical to mouse PTPR-kappa. Northern blotting revealed that PTPR-kappa is expressed as a 7.0-kb transcript in a variety of tissues. Fuchs et al. (1996) also used degenerate PCR to clone human PTPR-kappa. Northern blotting revealed expression of PTPR-kappa in mammary carcinoma cell lines as well as in various tissues. Fuchs et al. (1996) noted that PTPR-kappa has several structural features, such as a MAM domain, an Ig-like domain, and fibronectin repeats, suggesting that it could be involved in cell adhesion. They showed that PTPR-kappa forms a

complex with beta-catenin (OMIM Ref. No. 116806) and gamma-catenin/plakoglobin (OMIM Ref. No. 173325).

They also showed that PTPR-kappa expression is dependent on cell density and that it colocalizes with catenins at adherens junctions. These findings suggest that PTPR-kappa may have a role in the regulation of processes involving cell contact and adhesion.

[61484] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[61485] Fuchs, M.; Muller, T.; Lerch, M. M.; Ullrich, A. : Association of human protein-tyrosine phosphatase kappa with members of the armadillo family. J. Biol. Chem. 271: 16712-16719, 1996. ; and

[61486] Yang, Y.; Gil, M. C.; Choi, E. Y.; Park, S. H.; Pyun, K. H.; Ha, H. : Molecular cloning and chromosomal localization of a human gene homologous to the murine R-PTP-kappa, a receptor-type.

[61487] Further studies establishing the function and utilities of PTPRK are found in John Hopkins OMIM database record ID 602545, and in cited publications numbered 5873-5875 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein

Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_002848) is another VGAM1858 host target gene. PTPRO BINDING SITE1 through PTPRO BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRO, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE1 through PTPRO BINDING SITE5, designated SEQ ID:8739, SEQ ID:25004, SEQ ID:25012, SEQ ID:25021 and SEQ ID:25031 respectively, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61488] Another function of VGAM1858 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_002848), a gene which may function as a cell contact receptor that mediates and controls cell-cell signals. Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM140.Vasoactive Intestinal Peptide Receptor 1 (VIPR1, Accession NM\_004624) is another VGAM1858 host target gene. VIPR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VIPR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VIPR1 BINDING SITE, designated SEQ ID:10991, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61489] Another function of VGAM1858 is therefore inhibition of Vasoactive Intestinal Peptide Receptor 1 (VIPR1, Accession NM\_004624), a gene which binds vip and is mediated by g proteins which activate adenylyl cyclase. Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIPR1. The function of VIPR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM548.Chromosome 22 Open Reading Frame 19 (C22orf19, Accession NM\_003678) is another VGAM1858 host target gene. C22orf19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by C22orf19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf19 BINDING SITE, designated SEQ ID:9774, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61490] Another function of VGAM1858 is therefore inhibition of Chromosome 22 Open Reading Frame 19 (C22orf19, Accession NM\_003678). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf19. DKFZp547D155 (Accession XM\_046977) is another VGAM1858 host target gene. DKFZp547D155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547D155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547D155 BINDING SITE, designated SEQ ID:34869, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61491] Another function of VGAM1858 is therefore inhibition of DKFZp547D155 (Accession XM\_046977). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547D155. E74-like Factor 2 (ets domain transcription factor) (ELF2, Accession NM\_006874) is another VGAM1858 host target gene. ELF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELF2 BINDING SITE, designated SEQ ID:13744, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61492] Another function of VGAM1858 is therefore inhibition of E74-like Factor 2 (ets domain transcription factor) (ELF2, Accession NM\_006874). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELF2. FLJ10648 (Accession NM\_018167) is another VGAM1858 host target gene. FLJ10648 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ10648, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10648 BINDING SITE, designated SEQ ID:19985, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61493] Another function of VGAM1858 is therefore inhibition of FLJ10648 (Accession NM\_018167). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10648. FLJ20432 (Accession NM\_017819) is another VGAM1858 host target gene. FLJ20432 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20432 BINDING SITE, designated SEQ ID:19466, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61494] Another function of VGAM1858 is therefore inhibition of FLJ20432 (Accession NM\_017819). Accordingly, utilities of

VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20432. Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM\_002077) is another VGAM1858 host target gene. GOLGA1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GOLGA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA1 BINDING SITE, designated SEQ ID:7862, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61495] Another function of VGAM1858 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM\_002077). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA1. KIAA0193 (Accession NM\_014766) is another VGAM1858 host target gene. KIAA0193 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0193 BINDING SITE, designated SEQ ID:16543, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61496] Another function of VGAM1858 is therefore inhibition of KIAA0193 (Accession NM\_014766). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0193. KIAA0746 (Accession XM\_045277) is another VGAM1858 host target gene. KIAA0746 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0746, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0746 BINDING SITE, designated SEQ ID:34414, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61497] Another function of VGAM1858 is therefore inhibition of KIAA0746 (Accession XM\_045277). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0746. KIAA1041 (Accession NM\_014947) is another VGAM1858 host target gene. KIAA1041 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1041, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1041 BINDING SITE, designated SEQ ID:17264, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61498] Another function of VGAM1858 is therefore inhibition of KIAA1041 (Accession NM\_014947). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1041. KIAA1219 (Accession XM\_028835) is another VGAM1858 host target gene. KIAA1219 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1219 BINDING SITE, designated SEQ ID:30758, to the nucleotide sequence of VGAM1858 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4569.

[61499] Another function of VGAM1858 is therefore inhibition of KIAA1219 (Accession XM\_028835). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1219. Leucine Rich Repeat (in FLII) Interacting Protein 1 (LRRFIP1, Accession NM\_004735) is another VGAM1858 host target gene. LRRFIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRRFIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRRFIP1 BINDING SITE, designated SEQ ID:11120, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61500] Another function of VGAM1858 is therefore inhibition of Leucine Rich Repeat (in FLII) Interacting Protein 1 (LRRFIP1, Accession NM\_004735). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRRFIP1. NIR3 (Accession XM\_038799) is another VGAM1858 host target gene. NIR3 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by NIR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIR3 BINDING SITE, designated SEQ ID:32929, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61501] Another function of VGAM1858 is therefore inhibition of NIR3 (Accession XM\_038799). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIR3. p21(CDKN1A)-activated Kinase 6 (PAK6, Accession NM\_020168) is another VGAM1858 host target gene. PAK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAK6 BINDING SITE, designated SEQ ID:21392, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61502] Another function of VGAM1858 is therefore inhibition of



p21(CDKN1A)-activated Kinase 6 (PAK6, Accession NM\_020168). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK6. Syntaphilin (SNPH, Accession NM\_014723) is another VGAM1858 host target gene. SNPH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNPH BINDING SITE, designated SEQ ID:16296, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61503] Another function of VGAM1858 is therefore inhibition of Syntaphilin (SNPH, Accession NM\_014723). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNPH. TP53TG3 (Accession NM\_015369) is another VGAM1858 host target gene. TP53TG3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TP53TG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of TP53TG3 BINDING SITE, designated SEQ ID:17671, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61504] Another function of VGAM1858 is therefore inhibition of TP53TG3 (Accession NM\_015369). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP53TG3. Ubiquitin Specific Protease 24 (USP24, Accession XM\_165973) is another VGAM1858 host target gene. USP24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP24 BINDING SITE, designated SEQ ID:43818, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61505] Another function of VGAM1858 is therefore inhibition of Ubiquitin Specific Protease 24 (USP24, Accession XM\_165973). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with USP24. LOC151571 (Accession XM\_098088) is another VGAM1858 host target gene. LOC151571 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151571, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151571 BINDING SITE, designated SEQ ID:41372, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61506] Another function of VGAM1858 is therefore inhibition of LOC151571 (Accession XM\_098088). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151571. LOC196337 (Accession XM\_113696) is another VGAM1858 host target gene. LOC196337 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196337 BINDING SITE, designated SEQ ID:42359, to

the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61507] Another function of VGAM1858 is therefore inhibition of LOC196337 (Accession XM\_113696). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196337. LOC221341 (Accession XM\_167239) is another VGAM1858 host target gene. LOC221341 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221341, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221341 BINDING SITE, designated SEQ ID:44619, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61508] Another function of VGAM1858 is therefore inhibition of LOC221341 (Accession XM\_167239). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221341. LOC54505 (Accession XM\_042110) is another VGAM1858 host target gene. LOC54505 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC54505, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC54505 BINDING SITE, designated SEQ ID:33695, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61509] Another function of VGAM1858 is therefore inhibition of LOC54505 (Accession XM\_042110). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC54505. LOC54516 (Accession NM\_019041) is another VGAM1858 host target gene. LOC54516 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC54516, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC54516 BINDING SITE, designated SEQ ID:21123, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61510] Another function of VGAM1858 is therefore inhibition of LOC54516 (Accession NM\_019041). Accordingly, utilities

of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC54516. LOC90917 (Accession XM\_034861) is another VGAM1858 host target gene. LOC90917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90917 BINDING SITE, designated SEQ ID:32170, to the nucleotide sequence of VGAM1858 RNA, herein designated VGAM RNA, also designated SEQ ID:4569.

[61511] Another function of VGAM1858 is therefore inhibition of LOC90917 (Accession XM\_034861). Accordingly, utilities of VGAM1858 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90917. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1859 (VGAM1859) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61512] VGAM1859 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1859 was detected is described hereinabove with reference to Figs. 1–8.

[61513] VGAM1859 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rice Yellow Stunt Virus. VGAM1859 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61514] VGAM1859 gene encodes a VGAM1859 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1859 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1859 precursor RNA is designated SEQ ID:1845, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1845 is located at position 3094 relative to the genome of Rice Yellow Stunt Virus.

[61515] VGAM1859 precursor RNA folds onto itself, forming VGAM1859 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61516] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1859 folded precursor RNA into VGAM1859 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM1859 RNA is designated SEQ ID:4570, and is provided hereinbelow with reference to the sequence listing part.

[61517] VGAM1859 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1859 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1859 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated



5`UTR, PROTEIN CODING and 3`UTR respectively.

[61518] VGAM1859 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1859 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1859 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1859 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1859 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61519] The complementary binding of VGAM1859 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1859 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1859 host target RNA into VGAM1859 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61520] It is appreciated that VGAM1859 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1859 host target genes. The mRNA of each one of this plurality of VGAM1859 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1859 RNA, herein designated VGAM RNA, and which when bound by VGAM1859 RNA causes inhibition of translation of respective one or more VGAM1859 host target proteins.

[61521] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1859 gene, herein designated VGAM GENE, on one or more VGAM1859 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61522] It is yet further appreciated that a function of VGAM1859 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of viral infection by Rice Yellow Stunt Virus. Specific functions, and accordingly utilities, of VGAM1859 correlate with, and may be deduced from, the identity of the host target genes which VGAM1859 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61523] Nucleotide sequences of the VGAM1859 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1859 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1859 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1859 are further  
described hereinbelow with reference to Table 1.

[61524] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1859 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1859 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[61525] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1859 gene, herein designated VGAM is  
inhibition of expression of VGAM1859 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1859 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1859  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[61526] Histone Deacetylase 4 (HDAC4, Accession NM\_006037) is  
a VGAM1859 host target gene. HDAC4 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HDAC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC4 BINDING SITE, designated SEQ ID:12669, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61527] A function of VGAM1859 is therefore inhibition of Histone Deacetylase 4 (HDAC4, Accession NM\_006037), a gene which is responsible for the deacetylation of lysine residues on the n-terminal part of the core histones and may mediate transcriptional regulation. Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC4. The function of HDAC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM264. High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483) is another VGAM1859 host target gene. HMGA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGA2, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGA2 BINDING SITE, designated SEQ ID:9570, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61528] Another function of VGAM1859 is therefore inhibition of High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483), a gene which may affect transcription and cell differentiation; shares common DNA-binding motif with other HMG HMG I/Y family members. Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGA2. The function of HMGA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 duncce homolog, *Drosophila*) (PDE4D, Accession XM\_056815) is another VGAM1859 host target gene. PDE4D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4D BINDING SITE, designated SEQ ID:36428, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61529] Another function of VGAM1859 is therefore inhibition of Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, *Drosophila*) (PDE4D, Accession XM\_056815), a gene which has similarity to *Drosophila* dnc, which is the affected protein in learning and memory mutant dunce. Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4D. The function of PDE4D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. ADMP (Accession NM\_145035) is another VGAM1859 host target gene. ADMP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADMP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADMP BINDING SITE,

designated SEQ ID:29655, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61530] Another function of VGAM1859 is therefore inhibition of ADMP (Accession NM\_145035). Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADMP. DKFZP586N0721 (Accession NM\_015400) is another VGAM1859 host target gene. DKFZP586N0721 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586N0721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586N0721 BINDING SITE, designated SEQ ID:17710, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61531] Another function of VGAM1859 is therefore inhibition of DKFZP586N0721 (Accession NM\_015400). Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586N0721. FLJ13096 (Accession NM\_025000)



is another VGAM1859 host target gene. FLJ13096 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13096 BINDING SITE, designated SEQ ID:24568, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61532] Another function of VGAM1859 is therefore inhibition of FLJ13096 (Accession NM\_025000). Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13096. FLJ22794 (Accession XM\_166220) is another VGAM1859 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44035, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61533] Another function of VGAM1859 is therefore inhibition of FLJ22794 (Accession XM\_166220). Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. KIAA0232 (Accession XM\_052627) is another VGAM1859 host target gene. KIAA0232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0232 BINDING SITE, designated SEQ ID:36038, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61534] Another function of VGAM1859 is therefore inhibition of KIAA0232 (Accession XM\_052627). Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0232. Mitogen-activated Protein Kinase 8 Interacting Protein 3 (MAPK8IP3, Accession NM\_033392) is another VGAM1859 host target gene. MAPK8IP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPK8IP3, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK8IP3 BINDING SITE, designated SEQ ID:27223, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61535] Another function of VGAM1859 is therefore inhibition of Mitogen-activated Protein Kinase 8 Interacting Protein 3 (MAPK8IP3, Accession NM\_033392). Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK8IP3. Testis-specific Kinase 2 (TESK2, Accession XM\_032399) is another VGAM1859 host target gene. TESK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TESK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TESK2 BINDING SITE, designated SEQ ID:31653, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61536] Another function of VGAM1859 is therefore inhibition of

Testis-specific Kinase 2 (TESK2, Accession XM\_032399). Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSK2. LOC150225 (Accession XM\_097870) is another VGAM1859 host target gene. LOC150225 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150225, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150225 BINDING SITE, designated SEQ ID:41194, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61537] Another function of VGAM1859 is therefore inhibition of LOC150225 (Accession XM\_097870). Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150225. LOC221814 (Accession XM\_168226) is another VGAM1859 host target gene. LOC221814 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221814, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221814 BINDING SITE, designated SEQ ID:45094, to the nucleotide sequence of VGAM1859 RNA, herein designated VGAM RNA, also designated SEQ ID:4570.

[61538] Another function of VGAM1859 is therefore inhibition of LOC221814 (Accession XM\_168226). Accordingly, utilities of VGAM1859 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221814. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1860 (VGAM1860) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61539] VGAM1860 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1860 was detected is described hereinabove with reference to Figs. 1-8.

[61540] VGAM1860 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rice Yellow Stunt Virus. VGAM1860 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[61541] VGAM1860 gene encodes a VGAM1860 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1860 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1860 precursor RNA is designated SEQ ID:1846, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1846 is located at position 9805 relative to the genome of Rice Yellow Stunt Virus.

[61542] VGAM1860 precursor RNA folds onto itself, forming VGAM1860 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61543] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1860 folded precursor RNA into VGAM1860

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1860 RNA is designated SEQ ID:4571, and is provided hereinbelow with reference to the sequence listing part.

[61544] VGAM1860 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1860 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1860 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61545] VGAM1860 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1860 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1860 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1860 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1860 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61546] The complementary binding of VGAM1860 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1860 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1860 host target RNA into VGAM1860 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM



host target protein is therefore outlined by a broken line.

[61547] It is appreciated that VGAM1860 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1860 host target genes. The mRNA of each one of this plurality of VGAM1860 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1860 RNA, herein designated VGAM RNA, and which when bound by VGAM1860 RNA causes inhibition of translation of respective one or more VGAM1860 host target proteins.

[61548] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1860 gene, herein designated VGAM GENE, on one or more VGAM1860 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61549] It is yet further appreciated that a function of VGAM1860 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of viral infection by Rice Yellow Stunt Virus. Specific functions, and accordingly utilities, of VGAM1860 correlate with, and may be deduced from, the identity of the host target genes which VGAM1860 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61550] Nucleotide sequences of the VGAM1860 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1860 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1860 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1860 are further described hereinbelow with reference to Table 1.

[61551] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1860 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1860 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61552] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1860 gene, herein designated VGAM is inhibition of expression of VGAM1860 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1860 correlate with, and may be deduced from, the identity of the target genes which VGAM1860 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61553] Beta-site APP-cleaving Enzyme 2 (BACE2, Accession NM\_138992) is a VGAM1860 host target gene. BACE2 BINDING SITE1 through BACE2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BACE2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BACE2 BINDING SITE1 through BACE2 BINDING SITE3, designated SEQ ID:29093,

SEQ ID:29091 and SEQ ID:14423 respectively, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61554] A function of VGAM1860 is therefore inhibition of Beta-site APP-cleaving Enzyme 2 (BACE2, Accession NM\_138992), a gene which cleaves intracellularly the b-secretase site of amyloid precursor protein. Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BACE2. The function of BACE2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM486. Sodium Channel, Nonvoltage-gated 1 Alpha (SCNN1A, Accession NM\_001038) is another VGAM1860 host target gene. SCNN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCNN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCNN1A BINDING SITE, designated SEQ ID:6703, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61555] Another function of VGAM1860 is therefore inhibition of Sodium Channel, Nonvoltage-gated 1 Alpha (SCNN1A, Accession NM\_001038). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCNN1A. Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM\_031184) is another VGAM1860 host target gene. SPON1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPON1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPON1 BINDING SITE, designated SEQ ID:31300, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61556] Another function of VGAM1860 is therefore inhibition of Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM\_031184). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPON1. Suppressor of Fused Homolog (Drosophila) (SUFU, Accession NM\_016169) is another VGAM1860 host target gene.

SUFU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SUFU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUFU BINDING SITE, designated SEQ ID:18252, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61557] Another function of VGAM1860 is therefore inhibition of Suppressor of Fused Homolog (Drosophila) (SUFU, Accession NM\_016169). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUFU. A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248) is another VGAM1860 host target gene. AKAP11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP11 BINDING SITE, designated SEQ ID:18373, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61558] Another function of VGAM1860 is therefore inhibition of A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP11. CHFR (Accession NM\_018223) is another VGAM1860 host target gene. CHFR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHFR BINDING SITE, designated SEQ ID:20147, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61559] Another function of VGAM1860 is therefore inhibition of CHFR (Accession NM\_018223). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHFR. FLJ10724 (Accession NM\_018194) is another VGAM1860 host target gene. FLJ10724 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10724, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10724 BINDING SITE, designated SEQ ID:20055, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61560] Another function of VGAM1860 is therefore inhibition of FLJ10724 (Accession NM\_018194). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10724. Histamine Receptor H4 (HRH4, Accession NM\_021624) is another VGAM1860 host target gene. HRH4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRH4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRH4 BINDING SITE, designated SEQ ID:22264, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61561] Another function of VGAM1860 is therefore inhibition of Histamine Receptor H4 (HRH4, Accession NM\_021624). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical condi-



tions associated with HRH4. KIAA0152 (Accession NM\_014730) is another VGAM1860 host target gene. KIAA0152 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0152 BINDING SITE, designated SEQ ID:16333, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61562] Another function of VGAM1860 is therefore inhibition of KIAA0152 (Accession NM\_014730). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0152. KIAA1871 (Accession XM\_028409) is another VGAM1860 host target gene. KIAA1871 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1871 BINDING SITE, designated SEQ ID:30706, to the

nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61563] Another function of VGAM1860 is therefore inhibition of KIAA1871 (Accession XM\_028409). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1871. MGC32043 (Accession NM\_144582) is another VGAM1860 host target gene. MGC32043 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC32043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC32043 BINDING SITE, designated SEQ ID:29391, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61564] Another function of VGAM1860 is therefore inhibition of MGC32043 (Accession NM\_144582). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC32043. MGC32104 (Accession NM\_144684) is another VGAM1860 host target gene. MGC32104 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by MGC32104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC32104 BINDING SITE, designated SEQ ID:29504, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61565] Another function of VGAM1860 is therefore inhibition of MGC32104 (Accession NM\_144684). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC32104. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM\_028840) is another VGAM1860 host target gene. PPP1R16B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R16B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R16B BINDING SITE, designated SEQ ID:30771, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61566] Another function of VGAM1860 is therefore inhibition of

Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM\_028840). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R16B. RAB1B, Member RAS Oncogene Family (RAB1B, Accession NM\_030981) is another VGAM1860 host target gene. RAB1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB1B BINDING SITE, designated SEQ ID:25245, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61567] Another function of VGAM1860 is therefore inhibition of RAB1B, Member RAS Oncogene Family (RAB1B, Accession NM\_030981). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB1B. SMT3 Suppressor of Mif Two 3 Homolog 2 (yeast) (SMT3H2, Accession NM\_006937) is another VGAM1860 host target gene. SMT3H2 BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by SMT3H2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMT3H2 BINDING SITE, designated SEQ ID:13820, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61568] Another function of VGAM1860 is therefore inhibition of SMT3 Suppressor of Mif Two 3 Homolog 2 (yeast) (SMT3H2, Accession NM\_006937). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMT3H2. TP53TG3 (Accession NM\_015369) is another VGAM1860 host target gene. TP53TG3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TP53TG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP53TG3 BINDING SITE, designated SEQ ID:17670, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61569] Another function of VGAM1860 is therefore inhibition of TP53TG3 (Accession NM\_015369). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP53TG3. LOC158581 (Accession XM\_098968) is another VGAM1860 host target gene. LOC158581 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158581, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158581 BINDING SITE, designated SEQ ID:42016, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61570] Another function of VGAM1860 is therefore inhibition of LOC166713 (Accession XM\_106174). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166713. LOC166713 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC166713, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166713 BINDING SITE, designated SEQ ID:42196, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61571] Another function of VGAM1860 is therefore inhibition of LOC166713 (Accession XM\_106174). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166713. LOC196074 (Accession XM\_113647) is another VGAM1860 host target gene. LOC196074 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196074 BINDING SITE, designated SEQ ID:42321, to the nucleotide sequence of VGAM1860 RNA, herein designated VGAM RNA, also designated SEQ ID:4571.

[61572] Another function of VGAM1860 is therefore inhibition of LOC196074 (Accession XM\_113647). Accordingly, utilities of VGAM1860 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196074. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1861 (VGAM1861) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61573] VGAM1861 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1861 was detected is described hereinabove with reference to Figs. 1–8.

[61574] VGAM1861 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rice Yellow Stunt Virus. VGAM1861 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61575] VGAM1861 gene encodes a VGAM1861 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1861 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1861 precursor RNA is designated SEQ ID:1847, and is provided hereinbelow with ref–



erence to the sequence listing part. Nucleotide sequence SEQ ID:1847 is located at position 11283 relative to the genome of Rice Yellow Stunt Virus.

- [61576] VGAM1861 precursor RNA folds onto itself, forming VGAM1861 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [61577] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1861 folded precursor RNA into VGAM1861 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1861 RNA is designated SEQ ID:4572, and is provided hereinbelow with reference to the sequence listing part.

[61578] VGAM1861 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1861 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1861 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61579] VGAM1861 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1861 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1861 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1861 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1861 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[61580] The complementary binding of VGAM1861 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1861 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1861 host target RNA into VGAM1861 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61581] It is appreciated that VGAM1861 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1861 host target genes. The mRNA of each one of this plurality of VGAM1861 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1861 RNA, herein designated VGAM RNA, and which when bound by VGAM1861 RNA causes

inhibition of translation of respective one or more VGAM1861 host target proteins.

[61582] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1861 gene, herein designated VGAM GENE, on one or more VGAM1861 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61583] It is yet further appreciated that a function of VGAM1861 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1861 include diagnosis, prevention and

treatment of viral infection by Rice Yellow Stunt Virus. Specific functions, and accordingly utilities, of VGAM1861 correlate with, and may be deduced from, the identity of the host target genes which VGAM1861 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61584] Nucleotide sequences of the VGAM1861 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1861 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1861 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1861 are further described hereinbelow with reference to Table 1.

[61585] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1861 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1861 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61586] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1861 gene, herein designated VGAM is inhibition of expression of VGAM1861 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1861 correlate with, and may be deduced from, the identity of the target genes which VGAM1861 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61587] FLJ12838 (Accession NM\_024641) is a VGAM1861 host target gene. FLJ12838 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12838, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12838 BINDING SITE, designated SEQ ID:23922, to the nucleotide sequence of VGAM1861 RNA, herein designated VGAM RNA, also designated SEQ ID:4572.

[61588] A function of VGAM1861 is therefore inhibition of FLJ12838 (Accession NM\_024641). Accordingly, utilities of VGAM1861 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12838. LOC253971 (Accession XM\_171197) is another VGAM1861 host target gene. LOC253971 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253971, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253971 BINDING SITE, designated SEQ ID:45986, to the nucleotide sequence of VGAM1861 RNA, herein designated VGAM RNA, also designated SEQ ID:4572.

[61589] Another function of VGAM1861 is therefore inhibition of LOC253971 (Accession XM\_171197). Accordingly, utilities of VGAM1861 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253971. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1862 (VGAM1862) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61590] VGAM1862 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1862 was detected is described hereinabove with reference to Figs. 1–8.

[61591] VGAM1862 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lactate Dehydrogenase–elevat–

ing Virus. VGAM1862 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61592] VGAM1862 gene encodes a VGAM1862 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1862 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1862 precursor RNA is designated SEQ ID:1848, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1848 is located at position 5398 relative to the genome of Lactate Dehydrogenase-elevating Virus.

[61593] VGAM1862 precursor RNA folds onto itself, forming VGAM1862 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61594] An enzyme complex designated DICER COMPLEX, `dices`



the VGAM1862 folded precursor RNA into VGAM1862 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1862 RNA is designated SEQ ID:4573, and is provided hereinbelow with reference to the sequence listing part.

[61595] VGAM1862 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1862 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1862 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61596] VGAM1862 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1862 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1862 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1862 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1862 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61597] The complementary binding of VGAM1862 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1862 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1862 host target RNA into VGAM1862 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61598] It is appreciated that VGAM1862 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1862 host target genes. The mRNA of each one of this plurality of VGAM1862 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1862 RNA, herein designated VGAM RNA, and which when bound by VGAM1862 RNA causes inhibition of translation of respective one or more VGAM1862 host target proteins.

[61599] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1862 gene, herein designated VGAM GENE, on one or more VGAM1862 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61600] It is yet further appreciated that a function of VGAM1862 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of viral infection by Lactate Dehydrogenase-elevating Virus. Specific functions, and accordingly utilities, of VGAM1862 correlate with, and may be deduced from, the identity of the host target genes which VGAM1862 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61601] Nucleotide sequences of the VGAM1862 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1862 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1862 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1862 are further described hereinbelow with reference to Table 1.

[61602] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1862 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1862 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61603] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1862 gene, herein designated VGAM is inhibition of expression of VGAM1862 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1862 correlate with, and may be deduced from, the identity of the target genes which VGAM1862 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61604] BTB and CNC Homology 1, Basic Leucine Zipper Transcription Factor 2 (BACH2, Accession NM\_021813) is a VGAM1862 host target gene. BACH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BACH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BACH2 BIND-

ING SITE, designated SEQ ID:22382, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61605] A function of VGAM1862 is therefore inhibition of BTB and CNC Homology 1, Basic Leucine Zipper Transcription Factor 2 (BACH2, Accession NM\_021813), a gene which acts as repressor or activator, binds to maf recognition elements. Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BACH2. The function of BACH2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM331.C-type Lectin, Superfamily Member 12 (CLECSF12, Accession XM\_084768) is another VGAM1862 host target gene. CLECSF12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLECSF12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF12 BINDING SITE, designated SEQ ID:37686, to the nucleotide sequence of VGAM1862 RNA,

herein designated VGAM RNA, also designated SEQ ID:4573.

[61606] Another function of VGAM1862 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 12 (CLECSF12, Accession XM\_084768), a gene which is a pattern-recognition receptor . Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF12. The function of CLECSF12 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM121.Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM\_033096) is another VGAM1862 host target gene. CLTCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLTCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLTCL1 BINDING SITE, designated SEQ ID:31839, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61607] Another function of VGAM1862 is therefore inhibition of Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM\_033096), a gene which is involved in vesicle budding. Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLTCL1. The function of CLTCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42. Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262) is another VGAM1862 host target gene. HS2ST1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HS2ST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS2ST1 BINDING SITE, designated SEQ ID:14572, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61608] Another function of VGAM1862 is therefore inhibition of Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262). Accordingly, utilities of VGAM1862 in-



clude diagnosis, prevention and treatment of diseases and clinical conditions associated with HS2ST1. Potassium Voltage-gated Channel, Shaker-related Subfamily, Beta Member 2 (KCNAB2, Accession NM\_003636) is another VGAM1862 host target gene. KCNAB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNAB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNAB2 BINDING SITE, designated SEQ ID:9709, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61609] Another function of VGAM1862 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Beta Member 2 (KCNAB2, Accession NM\_003636), a gene which is the beta subunit of shaker voltage-gated potassium channels. Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNAB2. The function of KCNAB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM659.Transcription Factor-like 4 (TCFL4, Accession XM\_032817) is another VGAM1862 host target gene. TCFL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCFL4 BINDING SITE, designated SEQ ID:31771, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61610] Another function of VGAM1862 is therefore inhibition of Transcription Factor-like 4 (TCFL4, Accession XM\_032817), a gene which interacts with Mad and represses transcription by recruiting the Sin3A-histone deacetylase corepressor complex. Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCFL4. The function of TCFL4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172.Thyroid Hormone Receptor, Beta (erythroblastic leukemia viral (v-erb-a) Oncogene Ho-

molog 2, Avian) (THRB, Accession NM\_000461) is another VGAM1862 host target gene. THRB BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by THRB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THRB BINDING SITE, designated SEQ ID:6077, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61611] Another function of VGAM1862 is therefore inhibition of Thyroid Hormone Receptor, Beta (erythroblastic leukemia viral (v-erb-a) Oncogene Homolog 2, Avian) (THRB, Accession NM\_000461). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THRB. Tetratricopeptide Repeat Domain 3 (TTC3, Accession NM\_003316) is another VGAM1862 host target gene. TTC3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TTC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of TTC3 BINDING SITE, designated SEQ ID:9317, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61612] Another function of VGAM1862 is therefore inhibition of Tetratricopeptide Repeat Domain 3 (TTC3, Accession NM\_003316), a gene which contains tetratricopeptide repeat (TPR) motifs. Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTC3. The function of TTC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM699. Zinc Finger Protein 124 (HZF-16) (ZNF124, Accession NM\_003431) is another VGAM1862 host target gene. ZNF124 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF124, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF124 BINDING SITE, designated SEQ ID:9482, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61613] Another function of VGAM1862 is therefore inhibition of Zinc Finger Protein 124 (HZF-16) (ZNF124, Accession NM\_003431). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF124. A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248) is another VGAM1862 host target gene. AKAP11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP11 BINDING SITE, designated SEQ ID:18376, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61614] Another function of VGAM1862 is therefore inhibition of A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP11. C1q and Tumor Necrosis Factor Related Protein 2 (C1QTNF2, Accession NM\_031908) is another VGAM1862 host target gene. C1QTNF2 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by C1QTNF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QTNF2 BINDING SITE, designated SEQ ID:25652, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61615] Another function of VGAM1862 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 2 (C1QTNF2, Accession NM\_031908). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF2. Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM\_114191) is another VGAM1862 host target gene. C21orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf108 BINDING SITE, designated SEQ ID:42773, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA,

also designated SEQ ID:4573.

[61616] Another function of VGAM1862 is therefore inhibition of Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM\_114191). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf108. Collagen, Type XII, Alpha 1 (COL12A1, Accession NM\_080645) is another VGAM1862 host target gene. COL12A1 BINDING SITE1 and COL12A1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL12A1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL12A1 BINDING SITE1 and COL12A1 BINDING SITE2, designated SEQ ID:27937 and SEQ ID:10590 respectively, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61617] Another function of VGAM1862 is therefore inhibition of Collagen, Type XII, Alpha 1 (COL12A1, Accession NM\_080645). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL12A1. DKFZP667O116

(Accession XM\_168586) is another VGAM1862 host target gene. DKFZP667O116 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP667O116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP667O116 BINDING SITE, designated SEQ ID:45266, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61618] Another function of VGAM1862 is therefore inhibition of DKFZP667O116 (Accession XM\_168586). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP667O116. FLJ10687 (Accession NM\_018178) is another VGAM1862 host target gene. FLJ10687 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10687 BINDING SITE, designated SEQ ID:20011, to the nucleotide sequence of VGAM1862 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4573.

[61619] Another function of VGAM1862 is therefore inhibition of FLJ10687 (Accession NM\_018178). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10687. FLJ14260 (Accession NM\_025027) is another VGAM1862 host target gene. FLJ14260 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14260, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14260 BINDING SITE, designated SEQ ID:24619, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61620] Another function of VGAM1862 is therefore inhibition of FLJ14260 (Accession NM\_025027). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14260. FLJ20445 (Accession NM\_017824) is another VGAM1862 host target gene. FLJ20445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20445, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20445 BINDING SITE, designated SEQ ID:19476, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61621] Another function of VGAM1862 is therefore inhibition of FLJ20445 (Accession NM\_017824). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20445. FLJ20972 (Accession NM\_025030) is another VGAM1862 host target gene. FLJ20972 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20972, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20972 BINDING SITE, designated SEQ ID:24628, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61622] Another function of VGAM1862 is therefore inhibition of FLJ20972 (Accession NM\_025030). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20972. FLJ21432 (Accession NM\_024551) is another VGAM1862 host target gene. FLJ21432 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21432 BINDING SITE, designated SEQ ID:23763, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61623] Another function of VGAM1862 is therefore inhibition of FLJ21432 (Accession NM\_024551). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21432. HU-K4 (Accession NM\_012268) is another VGAM1862 host target gene. HU-K4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HU-K4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HU-K4 BINDING SITE, designated SEQ ID:14591, to the nucleotide sequence of

VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61624] Another function of VGAM1862 is therefore inhibition of HU-K4 (Accession NM\_012268). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HU-K4. HZFW1 (Accession NM\_025236) is another VGAM1862 host target gene. HZFW1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HZFW1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HZFW1 BINDING SITE, designated SEQ ID:24914, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61625] Another function of VGAM1862 is therefore inhibition of HZFW1 (Accession NM\_025236). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HZFW1. KIAA0237 (Accession NM\_014747) is another VGAM1862 host target gene. KIAA0237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16448, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61626] Another function of VGAM1862 is therefore inhibition of KIAA0237 (Accession NM\_014747). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. KIAA0322 (Accession XM\_166591) is another VGAM1862 host target gene. KIAA0322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0322 BINDING SITE, designated SEQ ID:44563, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61627] Another function of VGAM1862 is therefore inhibition of KIAA0322 (Accession XM\_166591). Accordingly, utilities

of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0322. KIAA1775 (Accession NM\_033100) is another VGAM1862 host target gene. KIAA1775 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1775, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1775 BINDING SITE, designated SEQ ID:26946, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61628] Another function of VGAM1862 is therefore inhibition of KIAA1775 (Accession NM\_033100). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1775. KIAA1948 (Accession XM\_091984) is another VGAM1862 host target gene. KIAA1948 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1948, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1948 BINDING SITE, designated SEQ ID:40075, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61629] Another function of VGAM1862 is therefore inhibition of KIAA1948 (Accession XM\_091984). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1948. Nuclear Cap Binding Protein Subunit 2, 20kDa (NCBP2, Accession NM\_007362) is another VGAM1862 host target gene. NCBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCBP2 BINDING SITE, designated SEQ ID:14294, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61630] Another function of VGAM1862 is therefore inhibition of Nuclear Cap Binding Protein Subunit 2, 20kDa (NCBP2, Accession NM\_007362). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCBP2.

PNPASE (Accession XM\_048088) is another VGAM1862 host target gene. PNPASE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PNPASE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PNPASE BINDING SITE, designated SEQ ID:35100, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61631] Another function of VGAM1862 is therefore inhibition of PNPASE (Accession XM\_048088). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PNPASE. SBBI31 (Accession NM\_014035) is another VGAM1862 host target gene. SBBI31 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SBBI31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SBBI31 BINDING SITE, designated SEQ ID:15267, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also des-



ignated SEQ ID:4573.

[61632] Another function of VGAM1862 is therefore inhibition of SBBI31 (Accession NM\_014035). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SBBI31. TXI1 (Accession NM\_018430) is another VGAM1862 host target gene. TXI1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TXI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TXI1 BINDING SITE, designated SEQ ID:20493, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61633] Another function of VGAM1862 is therefore inhibition of TXI1 (Accession NM\_018430). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TXI1. Zinc Finger Protein 17 (HPF3, KOX 10) (ZNF17, Accession XM\_091895) is another VGAM1862 host target gene. ZNF17 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF17,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF17 BINDING SITE, designated SEQ ID:40069, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61634] Another function of VGAM1862 is therefore inhibition of Zinc Finger Protein 17 (HPF3, KOX 10) (ZNF17, Accession XM\_091895). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF17. LOC120114 (Accession XM\_061871) is another VGAM1862 host target gene. LOC120114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120114 BINDING SITE, designated SEQ ID:37215, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61635] Another function of VGAM1862 is therefore inhibition of

LOC120114 (Accession XM\_061871). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120114. LOC122553 (Accession XM\_058630) is another VGAM1862 host target gene. LOC122553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122553, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122553 BINDING SITE, designated SEQ ID:36691, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61636] Another function of VGAM1862 is therefore inhibition of LOC122553 (Accession XM\_058630). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122553. LOC123242 (Accession XM\_063548) is another VGAM1862 host target gene. LOC123242 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC123242, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC123242 BINDING SITE, designated SEQ ID:37246, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61637] Another function of VGAM1862 is therefore inhibition of LOC123242 (Accession XM\_063548). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123242. LOC145815 (Accession XM\_096874) is another VGAM1862 host target gene. LOC145815 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145815, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145815 BINDING SITE, designated SEQ ID:40605, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61638] Another function of VGAM1862 is therefore inhibition of LOC145815 (Accession XM\_096874). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145815. LOC149448 (Accession XM\_097642) is an-

other VGAM1862 host target gene. LOC149448 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149448, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149448 BINDING SITE, designated SEQ ID:40991, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61639] Another function of VGAM1862 is therefore inhibition of LOC149448 (Accession XM\_097642). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149448. LOC153146 (Accession XM\_098319) is another VGAM1862 host target gene. LOC153146 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153146 BINDING SITE, designated SEQ ID:41578, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61640] Another function of VGAM1862 is therefore inhibition of LOC153146 (Accession XM\_098319). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153146. LOC153768 (Accession NM\_138492) is another VGAM1862 host target gene. LOC153768 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153768, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153768 BINDING SITE, designated SEQ ID:28844, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61641] Another function of VGAM1862 is therefore inhibition of LOC153768 (Accession NM\_138492). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153768. LOC157627 (Accession XM\_088347) is another VGAM1862 host target gene. LOC157627 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157627, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157627 BINDING SITE, designated SEQ ID:39618, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61642] Another function of VGAM1862 is therefore inhibition of LOC157627 (Accession XM\_088347). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157627. LOC196955 (Accession XM\_085210) is another VGAM1862 host target gene. LOC196955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196955 BINDING SITE, designated SEQ ID:37938, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61643] Another function of VGAM1862 is therefore inhibition of LOC196955 (Accession XM\_085210). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196955. LOC201824 (Accession XM\_114384) is another VGAM1862 host target gene. LOC201824 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201824 BINDING SITE, designated SEQ ID:42920, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61644] Another function of VGAM1862 is therefore inhibition of LOC201824 (Accession XM\_114384). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201824. LOC219654 (Accession XM\_166095) is another VGAM1862 host target gene. LOC219654 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219654, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219654 BINDING SITE, designated SEQ ID:43871, to the nucleotide sequence of VGAM1862 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4573.

[61645] Another function of VGAM1862 is therefore inhibition of LOC219654 (Accession XM\_166095). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219654. LOC222803 (Accession XM\_169907) is another VGAM1862 host target gene. LOC222803 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222803, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222803 BINDING SITE, designated SEQ ID:45305, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61646] Another function of VGAM1862 is therefore inhibition of LOC222803 (Accession XM\_169907). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222803. LOC257438 (Accession XM\_168338) is another VGAM1862 host target gene. LOC257438 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257438, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257438 BINDING SITE, designated SEQ ID:45109, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61647] Another function of VGAM1862 is therefore inhibition of LOC257438 (Accession XM\_168338). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257438. LOC90906 (Accession XM\_034809) is another VGAM1862 host target gene. LOC90906 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90906 BINDING SITE, designated SEQ ID:32155, to the nucleotide sequence of VGAM1862 RNA, herein designated VGAM RNA, also designated SEQ ID:4573.

[61648] Another function of VGAM1862 is therefore inhibition of LOC90906 (Accession XM\_034809). Accordingly, utilities of VGAM1862 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC90906. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1863 (VGAM1863) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61649] VGAM1863 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1863 was detected is described hereinabove with reference to Figs. 1–8.

[61650] VGAM1863 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM1863 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61651] VGAM1863 gene encodes a VGAM1863 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1863 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1863 precursor RNA is desig-

nated SEQ ID:1849, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1849 is located at position 121675 relative to the genome of Callitrichine Herpesvirus 3.

- [61652] VGAM1863 precursor RNA folds onto itself, forming VGAM1863 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [61653] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1863 folded precursor RNA into VGAM1863 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1863 RNA is designated SEQ ID:4574, and is provided hereinbelow with reference to the sequence

listing part.

[61654] VGAM1863 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1863 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1863 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61655] VGAM1863 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1863 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1863 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1863 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1863 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61656] The complementary binding of VGAM1863 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1863 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1863 host target RNA into VGAM1863 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61657] It is appreciated that VGAM1863 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1863 host target genes. The mRNA of each one of this plurality of VGAM1863 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1863 RNA, herein designated VGAM

RNA, and which when bound by VGAM1863 RNA causes inhibition of translation of respective one or more VGAM1863 host target proteins.

[61658] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1863 gene, herein designated VGAM GENE, on one or more VGAM1863 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61659] It is yet further appreciated that a function of VGAM1863 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1863 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1863 correlate with, and may be deduced from, the identity of the host target genes which VGAM1863 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61660] Nucleotide sequences of the VGAM1863 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1863 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1863 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1863 are further described hereinbelow with reference to Table 1.

[61661] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1863 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1863 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61662] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1863 gene, herein designated VGAM is



inhibition of expression of VGAM1863 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1863 correlate with, and may be deduced from, the identity of the target genes which VGAM1863 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61663] Asialoglycoprotein Receptor 1 (ASGR1, Accession NM\_001671) is a VGAM1863 host target gene. ASGR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ASGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASGR1 BINDING SITE, designated SEQ ID:7384, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61664] A function of VGAM1863 is therefore inhibition of Asialoglycoprotein Receptor 1 (ASGR1, Accession NM\_001671), a gene which mediates the endocytosis of plasma glycoproteins. Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASGR1. The function of ASGR1 and its association with various diseases and clinical con-

ditions, has been established by previous studies, as described hereinabove with reference to VGAM1345.ATPase, Ca++ Transporting, Plasma Membrane 4 (ATP2B4, Accession XM\_046775) is another VGAM1863 host target gene. ATP2B4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ATP2B4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP2B4 BINDING SITE, designated SEQ ID:34826, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61665] Another function of VGAM1863 is therefore inhibition of ATPase, Ca++ Transporting, Plasma Membrane 4 (ATP2B4, Accession XM\_046775). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP2B4. Guanine Nucleotide Binding Protein (G protein), Alpha Z Polypeptide (GNAZ, Accession NM\_002073) is another VGAM1863 host target gene. GNAZ BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GNAZ, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAZ BINDING SITE, designated SEQ ID:7845, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61666] Another function of VGAM1863 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Z Polypeptide (GNAZ, Accession NM\_002073), a gene which functions as modulator or transducer in various transmembrane signaling systems. Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAZ. The function of GNAZ and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1508. Potassium Inwardly-rectifying Channel, Subfamily J, Member 10 (KCNJ10, Accession NM\_002241) is another VGAM1863 host target gene. KCNJ10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNJ10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of KCNJ10 BINDING SITE, designated SEQ ID:8028, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61667] Another function of VGAM1863 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 10 (KCNJ10, Accession NM\_002241), a gene which may be responsible for potassium buffering action of glial cells in the brain. Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ10. The function of KCNJ10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM167.p21(CDKN1A)-activated Kinase 4 (PAK4, Accession NM\_005884) is another VGAM1863 host target gene. PAK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAK4 BINDING SITE, designated SEQ ID:12505, to the nucleotide sequence of VGAM1863 RNA, herein

designated VGAM RNA, also designated SEQ ID:4574.

[61668] Another function of VGAM1863 is therefore inhibition of p21(CDKN1A)-activated Kinase 4 (PAK4, Accession NM\_005884). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK4. Polycystic Kidney Disease 2-like 1 (PKD2L1, Accession NM\_016112) is another VGAM1863 host target gene. PKD2L1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PKD2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKD2L1 BINDING SITE, designated SEQ ID:18193, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61669] Another function of VGAM1863 is therefore inhibition of Polycystic Kidney Disease 2-like 1 (PKD2L1, Accession NM\_016112). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKD2L1. Arginine-glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM\_012102) is another VGAM1863 host target gene. RERE BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RERE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RERE BINDING SITE, designated SEQ ID:14404, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61670] Another function of VGAM1863 is therefore inhibition of Arginine–glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM\_012102), a gene which binds DRPLA and locates in the nucleus. Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RERE. The function of RERE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51. Selectin L (lymphocyte adhesion molecule 1) (SELL, Accession NM\_000655) is another VGAM1863 host target gene. SELL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SELL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SELL BINDING SITE, designated SEQ ID:6317, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61671] Another function of VGAM1863 is therefore inhibition of Selectin L (lymphocyte adhesion molecule 1) (SELL, Accession NM\_000655), a gene which is a cell surface adhesion protein. Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SELL. The function of SELL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM374. Snail Homolog 1 (Drosophila) (SNAI1, Accession NM\_005985) is another VGAM1863 host target gene. SNAI1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNAI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAI1 BINDING SITE, designated SEQ ID:12608, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61672] Another function of VGAM1863 is therefore inhibition of Snail Homolog 1 (Drosophila) (SNAI1, Accession NM\_005985). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAI1. SRGAP2 (Accession XM\_059095) is another VGAM1863 host target gene. SRGAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRGAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRGAP2 BINDING SITE, designated SEQ ID:36878, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61673] Another function of VGAM1863 is therefore inhibition of SRGAP2 (Accession XM\_059095). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRGAP2. Chromosome 1 Open Reading Frame 8 (C1orf8, Accession NM\_004872) is another VGAM1863 host target gene. C1orf8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by



C1orf8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf8 BINDING SITE, designated SEQ ID:11300, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61674] Another function of VGAM1863 is therefore inhibition of Chromosome 1 Open Reading Frame 8 (C1orf8, Accession NM\_004872). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf8. CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM\_004779) is another VGAM1863 host target gene. CNOT8 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CNOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT8 BINDING SITE, designated SEQ ID:11179, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61675] Another function of VGAM1863 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM\_004779). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT8. COP9 Constitutive Photomorphogenic Homolog Subunit 7B (Arabidopsis) (COPS7B, Accession NM\_022730) is another VGAM1863 host target gene. COPS7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COPS7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COPS7B BINDING SITE, designated SEQ ID:22931, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61676] Another function of VGAM1863 is therefore inhibition of COP9 Constitutive Photomorphogenic Homolog Subunit 7B (Arabidopsis) (COPS7B, Accession NM\_022730). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COPS7B. Discoidin Domain Receptor Family, Member 1 (DDR1, Accession NM\_013993) is another

VGAM1863 host target gene. DDR1 BINDING SITE1 through DDR1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DDR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDR1 BINDING SITE1 through DDR1 BINDING SITE3, designated SEQ ID:15179, SEQ ID:15181 and SEQ ID:7678 respectively, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61677] Another function of VGAM1863 is therefore inhibition of Discoidin Domain Receptor Family, Member 1 (DDR1, Accession NM\_013993). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDR1. FHX (Accession NM\_018416) is another VGAM1863 host target gene. FHX BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FHX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHX BINDING SITE, designated SEQ ID:20463,

to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61678] Another function of VGAM1863 is therefore inhibition of FHX (Accession NM\_018416). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHX. FLJ13241 (Accession NM\_025088) is another VGAM1863 host target gene. FLJ13241 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13241 BINDING SITE, designated SEQ ID:24710, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61679] Another function of VGAM1863 is therefore inhibition of FLJ13241 (Accession NM\_025088). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13241. FLJ14107 (Accession NM\_025026) is another VGAM1863 host target gene. FLJ14107 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by FLJ14107, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14107 BINDING SITE, designated SEQ ID:24617, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61680] Another function of VGAM1863 is therefore inhibition of FLJ14107 (Accession NM\_025026). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14107. FLJ22644 (Accession NM\_025098) is another VGAM1863 host target gene. FLJ22644 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22644 BINDING SITE, designated SEQ ID:24741, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61681] Another function of VGAM1863 is therefore inhibition of FLJ22644 (Accession NM\_025098). Accordingly, utilities of

VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22644. HXCP2 (Accession NM\_032579) is another VGAM1863 host target gene. HXCP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HXCP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HXCP2 BINDING SITE, designated SEQ ID:26313, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61682] Another function of VGAM1863 is therefore inhibition of HXCP2 (Accession NM\_032579). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HXCP2. KIAA0275 (Accession NM\_014767) is another VGAM1863 host target gene. KIAA0275 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0275 BINDING SITE,

designated SEQ ID:16551, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61683] Another function of VGAM1863 is therefore inhibition of KIAA0275 (Accession NM\_014767). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0275. KIAA0537 (Accession NM\_014840) is another VGAM1863 host target gene. KIAA0537 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0537, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0537 BINDING SITE, designated SEQ ID:16864, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61684] Another function of VGAM1863 is therefore inhibition of KIAA0537 (Accession NM\_014840). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0537. KIAA1393 (Accession XM\_050793) is another VGAM1863 host target gene. KIAA1393 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1393, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1393 BINDING SITE, designated SEQ ID:35689, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61685] Another function of VGAM1863 is therefore inhibition of KIAA1393 (Accession XM\_050793). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1393. LIECG3 (Accession XM\_113371) is another VGAM1863 host target gene. LIECG3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIECG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIECG3 BINDING SITE, designated SEQ ID:42247, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61686] Another function of VGAM1863 is therefore inhibition of



LIECG3 (Accession XM\_113371). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIECG3. MGC4504 (Accession NM\_024111) is another VGAM1863 host target gene. MGC4504 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4504 BINDING SITE, designated SEQ ID:23559, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61687] Another function of VGAM1863 is therefore inhibition of MGC4504 (Accession NM\_024111). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4504. PL6 (Accession NM\_007024) is another VGAM1863 host target gene. PL6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PL6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PL6 BINDING SITE, designated SEQ ID:13883, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61688] Another function of VGAM1863 is therefore inhibition of PL6 (Accession NM\_007024). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PL6. Sema Domain, Transmembrane Domain (TM), and Cytoplasmic Domain, (semaphorin) 6C (SEMA6C, Accession NM\_030913) is another VGAM1863 host target gene. SEMA6C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEMA6C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA6C BINDING SITE, designated SEQ ID:25183, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61689] Another function of VGAM1863 is therefore inhibition of Sema Domain, Transmembrane Domain (TM), and Cytoplasmic Domain, (semaphorin) 6C (SEMA6C, Accession

NM\_030913). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA6C. TP53TG3 (Accession NM\_015369) is another VGAM1863 host target gene. TP53TG3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TP53TG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP53TG3 BINDING SITE, designated SEQ ID:17672, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61690] Another function of VGAM1863 is therefore inhibition of TP53TG3 (Accession NM\_015369). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP53TG3. LOC116113 (Accession XM\_166413) is another VGAM1863 host target gene. LOC116113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC116113 BINDING SITE, designated SEQ ID:44283, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61691] Another function of VGAM1863 is therefore inhibition of LOC116113 (Accession XM\_166413). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116113. LOC145757 (Accession XM\_085227) is another VGAM1863 host target gene. LOC145757 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145757, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145757 BINDING SITE, designated SEQ ID:37970, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61692] Another function of VGAM1863 is therefore inhibition of LOC145757 (Accession XM\_085227). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145757. LOC146988 (Accession XM\_097150) is an-

other VGAM1863 host target gene. LOC146988 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146988 BINDING SITE, designated SEQ ID:40777, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61693] Another function of VGAM1863 is therefore inhibition of LOC146988 (Accession XM\_097150). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146988. LOC148029 (Accession XM\_086014) is another VGAM1863 host target gene. LOC148029 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148029, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148029 BINDING SITE, designated SEQ ID:38443, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61694] Another function of VGAM1863 is therefore inhibition of LOC148029 (Accession XM\_086014). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148029. LOC148114 (Accession XM\_086050) is another VGAM1863 host target gene. LOC148114 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148114 BINDING SITE, designated SEQ ID:38466, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61695] Another function of VGAM1863 is therefore inhibition of LOC148114 (Accession XM\_086050). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148114. LOC157450 (Accession XM\_048209) is another VGAM1863 host target gene. LOC157450 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157450, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157450 BINDING SITE, designated SEQ ID:35145, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61696] Another function of VGAM1863 is therefore inhibition of LOC157450 (Accession XM\_048209). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157450. LOC157923 (Accession XM\_088422) is another VGAM1863 host target gene. LOC157923 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157923 BINDING SITE, designated SEQ ID:39684, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61697] Another function of VGAM1863 is therefore inhibition of LOC157923 (Accession XM\_088422). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC157923. LOC199986 (Accession XM\_117168) is another VGAM1863 host target gene. LOC199986 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199986, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199986 BINDING SITE, designated SEQ ID:43269, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61698] Another function of VGAM1863 is therefore inhibition of LOC199986 (Accession XM\_117168). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199986. LOC203043 (Accession XM\_121734) is another VGAM1863 host target gene. LOC203043 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203043 BINDING SITE, designated SEQ ID:43615, to the nucleotide sequence of VGAM1863 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4574.

[61699] Another function of VGAM1863 is therefore inhibition of LOC203043 (Accession XM\_121734). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203043. LOC221749 (Accession XM\_166341) is another VGAM1863 host target gene. LOC221749 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221749, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221749 BINDING SITE, designated SEQ ID:44179, to the nucleotide sequence of VGAM1863 RNA, herein designated VGAM RNA, also designated SEQ ID:4574.

[61700] Another function of VGAM1863 is therefore inhibition of LOC221749 (Accession XM\_166341). Accordingly, utilities of VGAM1863 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221749. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1864 (VGAM1864) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61701] VGAM1864 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1864 was detected is described hereinabove with reference to Figs. 1–8.

[61702] VGAM1864 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM1864 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61703] VGAM1864 gene encodes a VGAM1864 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1864 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1864 precursor RNA is designated SEQ ID:1850, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1850 is located at position 121062 relative to the genome of Callitrichine Herpesvirus 3.

[61704] VGAM1864 precursor RNA folds onto itself, forming

VGAM1864 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61705] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1864 folded precursor RNA into VGAM1864 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 64%) nucleotide sequence of VGAM1864 RNA is designated SEQ ID:4575, and is provided hereinbelow with reference to the sequence listing part.

[61706] VGAM1864 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1864 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1864 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61707] VGAM1864 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1864 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1864 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1864 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1864 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61708] The complementary binding of VGAM1864 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1864 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1864 host target RNA into VGAM1864 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61709] It is appreciated that VGAM1864 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1864 host target genes. The mRNA of each one of this plurality of VGAM1864 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1864 RNA, herein designated VGAM RNA, and which when bound by VGAM1864 RNA causes inhibition of translation of respective one or more VGAM1864 host target proteins.

[61710] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1864 gene, herein designated VGAM GENE, on one or more VGAM1864 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61711] It is yet further appreciated that a function of VGAM1864 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1864 correlate with, and may be deduced from, the identity of the host target genes which VGAM1864 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[61712] Nucleotide sequences of the VGAM1864 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1864 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1864 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1864 are further described hereinbelow with reference to Table 1.

[61713] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1864 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1864 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61714] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1864 gene, herein designated VGAM is inhibition of expression of VGAM1864 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1864 correlate with, and may be deduced from, the identity of the target genes which VGAM1864 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[61715] Adenylate Cyclase 8 (brain) (ADCY8, Accession NM\_001115) is a VGAM1864 host target gene. ADCY8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ADCY8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY8 BINDING SITE, designated SEQ ID:6788, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61716] A function of VGAM1864 is therefore inhibition of Adenylate Cyclase 8 (brain) (ADCY8, Accession NM\_001115), a gene which is a membrane-bound,  $\text{Ca}^{2+}$ -inhibitable adenylyl cyclase. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY8. The function of ADCY8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1169. AT-binding Transcription Factor 1 (ATBF1, Accession NM\_006885) is another VGAM1864 host target gene. ATBF1 BINDING SITE is HOST TARGET binding site



found in the 5` untranslated region of mRNA encoded by ATBF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATBF1 BINDING SITE, designated SEQ ID:13748, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61717] Another function of VGAM1864 is therefore inhibition of AT-binding Transcription Factor 1 (ATBF1, Accession NM\_006885). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATBF1. BCL2-like 2 (BCL2L2, Accession NM\_004050) is another VGAM1864 host target gene. BCL2L2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BCL2L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2L2 BINDING SITE, designated SEQ ID:10262, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61718] Another function of VGAM1864 is therefore inhibition of BCL2-like 2 (BCL2L2, Accession NM\_004050), a gene which promotes cell survival. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2L2. The function of BCL2L2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM431. Dishevelled, Dsh Homolog 1 (Drosophila) (DVL1, Accession XM\_001589) is another VGAM1864 host target gene. DVL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DVL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVL1 BINDING SITE, designated SEQ ID:29842, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61719] Another function of VGAM1864 is therefore inhibition of Dishevelled, Dsh Homolog 1 (Drosophila) (DVL1, Accession XM\_001589), a gene which may play a role in the signal transduction pathway. Accordingly, utilities of

VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL1. The function of DVL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. Eukaryotic Translation Initiation Factor 4E Binding Protein 2 (EIF4EBP2, Accession NM\_004096) is another VGAM1864 host target gene. EIF4EBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF4EBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4EBP2 BINDING SITE, designated SEQ ID:10302, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61720] Another function of VGAM1864 is therefore inhibition of Eukaryotic Translation Initiation Factor 4E Binding Protein 2 (EIF4EBP2, Accession NM\_004096), a gene which binds EIF4E and negatively regulates initiation of translation. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF4EBP2. The function of EIF4EBP2

and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM501. Engrailed Homolog 2 (EN2, Accession NM\_001427) is another VGAM1864 host target gene. EN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EN2 BINDING SITE, designated SEQ ID:7145, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61721] Another function of VGAM1864 is therefore inhibition of Engrailed Homolog 2 (EN2, Accession NM\_001427), a gene which may be required for normal cerebellar development; a homeobox protein, very strongly similar to murine En2. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EN2. The function of EN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. G Pro-

tein-coupled Receptor 85 (GPR85, Accession NM\_018970) is another VGAM1864 host target gene. GPR85 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR85, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR85 BINDING SITE, designated SEQ ID:21043, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61722] Another function of VGAM1864 is therefore inhibition of G Protein-coupled Receptor 85 (GPR85, Accession NM\_018970). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR85. Glutathione Peroxidase 3 (plasma) (GPX3, Accession NM\_002084) is another VGAM1864 host target gene. GPX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPX3 BINDING SITE, designated SEQ ID:7879, to the nucleotide sequence of

VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61723] Another function of VGAM1864 is therefore inhibition of Glutathione Peroxidase 3 (plasma) (GPX3, Accession NM\_002084), a gene which reduces lipid hydroperoxide and H<sub>2</sub>O<sub>2</sub> in plasma. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPX3. The function of GPX3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM225. High-mobility Group Box 2 (HMGB2, Accession NM\_002129) is another VGAM1864 host target gene. HMGB2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HMGB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGB2 BINDING SITE, designated SEQ ID:7907, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61724] Another function of VGAM1864 is therefore inhibition of

High-mobility Group Box 2 (HMGB2, Accession NM\_002129), a gene which binds to single-stranded DNA, unwinds double-stranded DNA, and increases transcription. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGB2. The function of HMGB2 has been established by previous studies. The high mobility group (HMG) proteins are localized in the nuclei of higher eukaryotes and occur in 3 families, 1 of which includes HMG1 (OMIM Ref. No. 163905) and HMG2. These proteins include a so-called HMG box which is involved in DNA binding. Both HMG1 and HMG2 proteins bind to single-stranded DNA, unwind double-stranded DNA, and increase transcription (Wanschura et al., 1996). By screening a human genomic library with the pig thymus cDNA coding for chromosomal protein HGM2, Shirakawa and Yoshida (1992) isolated a 4,341-bp fragment containing the entire gene encoding this protein. The gene was 2,665 bp long from the start site to the end of transcription and comprised 5 exons. Length of the mRNA predicted from the exons was 1,125 bp. The canonical 5-prime regulatory motifs, CCAAT, were present, whereas the TATA element was absent from the gene. The primary structure of

the human HMG2 protein consisted of 208 amino acid residues and was different from that of the pig HGM2 in only 2 amino acids; one was exchanged and the other was missing.

[61725] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[61726] Shirakawa, H.; Yoshida, M. : Structure of a gene coding for human HMG2 protein. J. Biol. Chem. 267: 6641–6645, 1992. ; and

[61727] Wanschura, S.; Schoenmakers, E. F. P. M.; Huysmans, C.; Bartnitzke, S.; Van de Ven, W. J. M.; Bullerdiek, J. : Mapping of the human HMG2 gene to 4q31. Genomics 31: 264–265, 1996.

[61728] Further studies establishing the function and utilities of HMGB2 are found in John Hopkins OMIM database record ID 163906, and in cited publications numbered 3009–3010 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Inositol 1,4,5–trisphosphate 3–kinase B (ITPKB, Accession NM\_002221) is another VGAM1864 host target gene. ITPKB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ITPKB,



corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPKB BINDING SITE, designated SEQ ID:7981, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61729] Another function of VGAM1864 is therefore inhibition of Inositol 1,4,5-trisphosphate 3-kinase B (ITPKB, Accession NM\_002221), a gene which is a type B inositol 1,4,5-triphosphate 3 kinase. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPKB. The function of ITPKB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1252. Potassium Voltage-gated Channel, Isk-related Family, Member 1-like (KCNE1L, Accession NM\_012282) is another VGAM1864 host target gene. KCNE1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNE1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of KCNE1L BINDING SITE, designated SEQ ID:14615, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61730] Another function of VGAM1864 is therefore inhibition of Potassium Voltage-gated Channel, Isk-related Family, Member 1-like (KCNE1L, Accession NM\_012282), a gene which is a potassium voltage-gated channel. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNE1L. The function of KCNE1L has been established by previous studies. Kv4 (KCND) proteins form voltage-activated A-type potassium ion channels and are prominent in the repolarization phase of the action potential. By screening a cardiac cDNA library and RT-PCR of human ventricular RNA, Kong et al. (1998) isolated a cDNA encoding KCND3. The deduced 637-amino acid protein shares 99% sequence homology with the rat homolog. KCND3 contains 6 transmembrane segments and intracellular N- and C-termini. RT-PCR and sequence analysis demonstrated the existence of a splice variant, KCND3L, with an insert encoding an additional 19 amino acids and containing a phosphorylation site. The shorter

isoform was designated KCND3S. Zhu et al. (1999) found that the KCND3L, KCND1 (OMIM Ref. No. 300281), and KCND2 (OMIM Ref. No. 600410) proteins share 60% sequence identity and 71% homology, with the least conservation in the C terminus. By Northern blot analysis, Kong et al. (1998) detected expression of an 8.5-kb transcript that is most abundant in brain and heart and is not detectable in kidney, liver, lung, pancreas, spleen, or skeletal muscle. By the same method, Isbrandt et al. (2000) found that expression within the brain is greatest in the cerebral cortex. By RT-PCR analysis, they found that the long transcript predominates in thalamus, caudate nucleus, white matter, and epiphysis, whereas the short transcript is more abundant in frontal cortex, occipital lobe, and cerebellar cortex. Dilks et al. (1999), who cloned KCND3 from human heart and brain, found by RT-PCR that only the long form of KCND3 is expressed in heart. Isbrandt et al. (2000) determined that the long form of the KCND3 gene contains 7 exons and spans at least 25 kb. The shorter isoform is encoded by 6 exons. Kong et al. (1998) and Dilks et al. (1999) found no differences in the splice variants in terms of their voltage dependence or inactivation kinetics in the basal state. The transient outward potas-

sium current,  $I(t_o)$ , is especially important during the early phase of repolarization in many species, including human, as it sets the plateau voltage of both the atrial and the ventricular action potential. KCND2 and/or KCND3 code for the primary alpha subunits responsible for  $I(t_o)$  (Tseng, 1999). In the human ventricle, KCND3 is the gene that encodes the  $K^+$  channel that underlies  $I(t_o)$  (Dixon et al., 1996). By FISH, Kong et al. (1998) mapped the KCND3 gene to chromosome 1p13.3. By radiation hybrid mapping, Postma et al. (2000) assigned the gene to 1p13

[61731] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[61732] Tseng, G.-N. : Molecular structure of cardiac  $I(t_o)$  channels: Kv4.2, Kv4.3, and other possibilities? Cardiovasc. Res. 41: 16–18, 1999. ; and

[61733] Zhu, X. R.; Wulf, A.; Schwarz, M.; Isbrandt, D.; Pongs, O. : Characterization of human Kv4.2 mediating a rapidly-inactivating transient voltage-sensitive  $K^+$  current. Receptors Channels.

[61734] Further studies establishing the function and utilities of KCNE1L are found in John Hopkins OMIM database record ID 300328, and in cited publications numbered 9151

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LPTM5 (Accession NM\_006762) is another VGAM1864 host target gene.

LPTM5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPTM5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPTM5 BINDING SITE, designated SEQ ID:13616, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61735] Another function of VGAM1864 is therefore inhibition of LPTM5 (Accession NM\_006762). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPTM5. Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM\_035037) is another VGAM1864 host target gene. LRP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LRP4 BINDING SITE, designated SEQ ID:32203, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61736] Another function of VGAM1864 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM\_035037). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP4. Neuralized-like (Drosophila) (NEURL, Accession NM\_004210) is another VGAM1864 host target gene. NEURL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEURL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEURL BINDING SITE, designated SEQ ID:10411, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61737] Another function of VGAM1864 is therefore inhibition of Neuralized-like (Drosophila) (NEURL, Accession NM\_004210). Accordingly, utilities of VGAM1864 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with NEURL. Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM\_002531) is another VGAM1864 host target gene. NTSR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NTSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTSR1 BINDING SITE, designated SEQ ID:8371, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61738] Another function of VGAM1864 is therefore inhibition of Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM\_002531), a gene which is associated with g proteins that activate a phosphatidylinositol- calcium second messenger system. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTSR1. The function of NTSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.Phosphoinositide-3-kinase, Regulatory Subunit,

Polypeptide 1 (p85 alpha) (PIK3R1, Accession XM\_043865) is another VGAM1864 host target gene. PIK3R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3R1 BINDING SITE, designated SEQ ID:34037, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61739] Another function of VGAM1864 is therefore inhibition of Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 1 (p85 alpha) (PIK3R1, Accession XM\_043865), a gene which acts as an adapter, for the insulin-stimulated increase in glucose uptake and glycogen synthesis. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3R1. The function of PIK3R1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM826. Placenta-specific 1 (PLAC1, Accession NM\_021796) is another VGAM1864 host target gene. PLAC1 BINDING SITE is HOST TARGET



binding site found in the 5` untranslated region of mRNA encoded by PLAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAC1 BINDING SITE, designated SEQ ID:22353, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61740] Another function of VGAM1864 is therefore inhibition of Placenta-specific 1 (PLAC1, Accession NM\_021796). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAC1. POU Domain, Class 4, Transcription Factor 1 (POU4F1, Accession NM\_006237) is another VGAM1864 host target gene. POU4F1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by POU4F1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU4F1 BINDING SITE, designated SEQ ID:12896, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61741] Another function of VGAM1864 is therefore inhibition of POU Domain, Class 4, Transcription Factor 1 (POU4F1, Accession NM\_006237), a gene which plays a role in the regulation of specific gene expression within a subset of neuronal lineages. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU4F1. The function of POU4F1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1026. RNA Binding Motif Protein 8A (RBM8A, Accession NM\_005105) is another VGAM1864 host target gene. RBM8A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RBM8A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBM8A BINDING SITE, designated SEQ ID:11580, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61742] Another function of VGAM1864 is therefore inhibition of RNA Binding Motif Protein 8A (RBM8A, Accession

NM\_005105), a gene which involves in the pathway of gene expression postsplicing nuclear preexport mRNPs, and newly exported cytoplasmic mRNPs. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBM8A. The function of RBM8A has been established by previous studies. Mago nashi (MAGOH; 602603), meaning grandchildless, is the homolog of a *Drosophila* protein required for normal germ plasm development in fly embryos. By performing a yeast 2-hybrid screen on a fetal brain cDNA library with MAGOH as the bait, Zhao et al. (2000) recovered a cDNA encoding RBM8. The 173-amino acid RBM8 protein is more than 93% identical to the mouse and zebrafish sequences, and the mouse differences are all accounted for by an 11-amino acid N-terminal insertion and another single-residue insertion in the mouse sequence. Exchange partner and GST pull-down assays confirmed the MAGOH-RBM8 interaction and showed that RBM8 is expressed as a 26-kD protein, slightly larger than the predicted mass of 23 kD. Northern blot analysis detected a major RBM8 transcript of less than 1.0 kb in all tissues tested, with weakest expression in pancreas and brain. By searching an EST database for

homologs of the gonadotropin-releasing hormone receptor (GNRHR; 138850), followed by 5-prime RACE on a skeletal muscle cDNA library, Conklin et al. (2000) identified a cDNA encoding RBM8. Northern blot analysis detected a major 0.9-kb transcript in all tissues tested. Sequence analysis of the 174-amino acid protein predicted an RNA-binding domain, which is composed of 2 amphipathic alpha helices packed against a 4-stranded beta sheet, and a C-terminal arg-rich segment.

[61743] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[61744] Conklin, D. C.; Rixon, M. W.; Kuestner, R. E.; Maurer, M. F.; Whitmore, T. E.; Millar, R. P. : Cloning and gene expression of a novel human ribonucleoprotein. *Biochim. Biophys. Acta* 1492: 465-469, 2000. ; and

[61745] Zhao, X.-F.; Nowak, N. J.; Shows, T. B.; Aplan, P. D. : MAGOH interacts with a novel RNA-binding protein. *Genomics* 63: 145-148, 2000.

[61746] Further studies establishing the function and utilities of RBM8A are found in John Hopkins OMIM database record ID 605313, and in cited publications numbered 745 and 7455-7457 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Receptor Tyrosine Kinase-like Orphan Receptor 2 (ROR2, Accession NM\_004560) is another VGAM1864 host target gene.

ROR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ROR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROR2 BINDING SITE, designated SEQ ID:10899, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61747] Another function of VGAM1864 is therefore inhibition of Receptor Tyrosine Kinase-like Orphan Receptor 2 (ROR2, Accession NM\_004560), a gene which may be involved in the early formation of the chondrocytes. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROR2. The function of ROR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM\_005628) is another VGAM1864 host target gene.

SLC1A5 BINDING SITE1 and SLC1A5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC1A5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A5 BINDING SITE1 and SLC1A5 BINDING SITE2, designated SEQ ID:12140 and SEQ ID:38400 respectively, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61748] Another function of VGAM1864 is therefore inhibition of Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM\_005628). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A5. Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 6 (SLC9A6, Accession NM\_006359) is another VGAM1864 host target gene. SLC9A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC9A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

SLC9A6 BINDING SITE, designated SEQ ID:13055, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61749] Another function of VGAM1864 is therefore inhibition of Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 6 (SLC9A6, Accession NM\_006359), a gene which is involved electroneutral exchange of protons for  $\text{Na}^+$  and  $\text{K}^+$  across the mitochondrial inner membrane. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC9A6. The function of SLC9A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM493. Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM\_031184) is another VGAM1864 host target gene. SPON1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPON1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPON1 BINDING SITE, designated SEQ ID:31301, to the nucleotide sequence of VGAM1864 RNA,

herein designated VGAM RNA, also designated SEQ ID:4575.

[61750] Another function of VGAM1864 is therefore inhibition of Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM\_031184). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPON1. Transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase) (TGM2, Accession NM\_004613) is another VGAM1864 host target gene. TGM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGM2 BINDING SITE, designated SEQ ID:10956, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61751] Another function of VGAM1864 is therefore inhibition of Transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase) (TGM2, Accession NM\_004613), a gene which catalyzes the cross-linking of proteins and the conjugation of polyamines to proteins.



Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGM2. The function of TGM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM899. Vascular Endothelial Growth Factor (VEGF, Accession NM\_003376) is another VGAM1864 host target gene. VEGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VEGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VEGF BINDING SITE, designated SEQ ID:9409, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61752] Another function of VGAM1864 is therefore inhibition of Vascular Endothelial Growth Factor (VEGF, Accession NM\_003376), a gene which induces endothelial cell proliferation and vascular permeability. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VEGF. The function of VEGF and its association with various dis-

eases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. Zinc Finger Protein 144 (Mel-18) (ZNF144, Accession NM\_007144) is another VGAM1864 host target gene. ZNF144 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF144, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF144 BINDING SITE, designated SEQ ID:13991, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61753] Another function of VGAM1864 is therefore inhibition of Zinc Finger Protein 144 (Mel-18) (ZNF144, Accession NM\_007144), a gene which is a transcriptional repressor and may play a role in the control of cell proliferation. Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF144. The function of ZNF144 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM380.13CDNA73

(Accession NM\_023037) is another VGAM1864 host target gene. 13CDNA73 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by 13CDNA73, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of 13CDNA73 BINDING SITE, designated SEQ ID:23322, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61754] Another function of VGAM1864 is therefore inhibition of 13CDNA73 (Accession NM\_023037). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with 13CDNA73. UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 6 (B3GNT6, Accession NM\_006876) is another VGAM1864 host target gene. B3GNT6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by B3GNT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GNT6 BINDING SITE, designated SEQ

ID:13745, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61755] Another function of VGAM1864 is therefore inhibition of UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 6 (B3GNT6, Accession NM\_006876). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GNT6. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294) is another VGAM1864 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26069, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61756] Another function of VGAM1864 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294). Accordingly,

utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. Claudin 4 (CLDN4, Accession NM\_001305) is another VGAM1864 host target gene. CLDN4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLDN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLDN4 BINDING SITE, designated SEQ ID:6987, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61757] Another function of VGAM1864 is therefore inhibition of Claudin 4 (CLDN4, Accession NM\_001305). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLDN4. CLIPR-59 (Accession NM\_015526) is another VGAM1864 host target gene. CLIPR-59 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLIPR-59, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIPR-59

BINDING SITE, designated SEQ ID:17790, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61758] Another function of VGAM1864 is therefore inhibition of CLIPR-59 (Accession NM\_015526). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIPR-59. DKFZP434C131 (Accession XM\_044630) is another VGAM1864 host target gene. DKFZP434C131 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434C131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C131 BINDING SITE, designated SEQ ID:34244, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61759] Another function of VGAM1864 is therefore inhibition of DKFZP434C131 (Accession XM\_044630). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C131. DKFZP434N1511 (Accession

XM\_166138) is another VGAM1864 host target gene. DKFZP434N1511 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434N1511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434N1511 BINDING SITE, designated SEQ ID:43935, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61760] Another function of VGAM1864 is therefore inhibition of DKFZP434N1511 (Accession XM\_166138). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434N1511. DKFZp547D155 (Accession XM\_046977) is another VGAM1864 host target gene. DKFZp547D155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547D155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547D155 BINDING SITE, designated SEQ ID:34866, to the nucleotide sequence of

VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61761] Another function of VGAM1864 is therefore inhibition of DKFZp547D155 (Accession XM\_046977). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547D155. DKFZP727C091 (Accession XM\_038689) is another VGAM1864 host target gene. DKFZP727C091 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP727C091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP727C091 BINDING SITE, designated SEQ ID:32902, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61762] Another function of VGAM1864 is therefore inhibition of DKFZP727C091 (Accession XM\_038689). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP727C091. DKFZp762P2111 (Accession XM\_098654) is another VGAM1864 host target gene. DK-



FZp762P2111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762P2111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762P2111 BINDING SITE, designated SEQ ID:41757, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61763] Another function of VGAM1864 is therefore inhibition of DKFZp762P2111 (Accession XM\_098654). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762P2111. DZIP1 (Accession NM\_014934) is another VGAM1864 host target gene. DZIP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DZIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DZIP1 BINDING SITE, designated SEQ ID:17232, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61764] Another function of VGAM1864 is therefore inhibition of DZIP1 (Accession NM\_014934). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DZIP1. Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295) is another VGAM1864 host target gene. EPB41L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPB41L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L1 BINDING SITE, designated SEQ ID:34939, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61765] Another function of VGAM1864 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L1. ETR101 (Accession XM\_051364) is another VGAM1864 host target gene. ETR101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by ETR101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ETR101 BINDING SITE, designated SEQ ID:35831, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61766] Another function of VGAM1864 is therefore inhibition of ETR101 (Accession XM\_051364). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ETR101. F-box Only Protein 21 (FBXO21, Accession NM\_033624) is another VGAM1864 host target gene. FBXO21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO21 BINDING SITE, designated SEQ ID:27319, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61767] Another function of VGAM1864 is therefore inhibition of

F-box Only Protein 21 (FBXO21, Accession NM\_033624). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO21. FLJ12541 (Accession NM\_022369) is another VGAM1864 host target gene. FLJ12541 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12541, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12541 BINDING SITE, designated SEQ ID:22758, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61768] Another function of VGAM1864 is therefore inhibition of FLJ12541 (Accession NM\_022369). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12541. FLJ12816 (Accession NM\_022060) is another VGAM1864 host target gene. FLJ12816 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12816, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12816 BINDING SITE, designated SEQ ID:22604, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61769] Another function of VGAM1864 is therefore inhibition of FLJ12816 (Accession NM\_022060). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12816. FLJ13189 (Accession NM\_024882) is another VGAM1864 host target gene. FLJ13189 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13189 BINDING SITE, designated SEQ ID:24329, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61770] Another function of VGAM1864 is therefore inhibition of FLJ13189 (Accession NM\_024882). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ13189. FLJ14803 (Accession NM\_032842) is another VGAM1864 host target gene. FLJ14803 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14803, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14803 BINDING SITE, designated SEQ ID:26626, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61771] Another function of VGAM1864 is therefore inhibition of FLJ14803 (Accession NM\_032842). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14803. FLJ20249 (Accession XM\_086573) is another VGAM1864 host target gene. FLJ20249 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20249 BINDING SITE, designated SEQ ID:38773, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM

RNA, also designated SEQ ID:4575.

[61772] Another function of VGAM1864 is therefore inhibition of FLJ20249 (Accession XM\_086573). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20249. FLJ20695 (Accession NM\_017929) is another VGAM1864 host target gene. FLJ20695 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20695, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20695 BINDING SITE, designated SEQ ID:19610, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61773] Another function of VGAM1864 is therefore inhibition of FLJ20695 (Accession NM\_017929). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20695. FLJ20886 (Accession XM\_170820) is another VGAM1864 host target gene. FLJ20886 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20886, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20886 BINDING SITE, designated SEQ ID:45596, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61774] Another function of VGAM1864 is therefore inhibition of FLJ20886 (Accession XM\_170820). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20886. FLJ21313 (Accession NM\_023927) is another VGAM1864 host target gene. FLJ21313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21313 BINDING SITE, designated SEQ ID:23407, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61775] Another function of VGAM1864 is therefore inhibition of FLJ21313 (Accession NM\_023927). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment



of diseases and clinical conditions associated with FLJ21313. FLJ23024 (Accession NM\_024936) is another VGAM1864 host target gene. FLJ23024 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23024 BINDING SITE, designated SEQ ID:24473, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61776] Another function of VGAM1864 is therefore inhibition of FLJ23024 (Accession NM\_024936). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23024. FLJ23441 (Accession NM\_024678) is another VGAM1864 host target gene. FLJ23441 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23441 BINDING SITE, designated SEQ ID:23988, to the nucleotide

sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61777] Another function of VGAM1864 is therefore inhibition of FLJ23441 (Accession NM\_024678). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23441. Forkhead Box J1 (FOXJ1, Accession NM\_001454) is another VGAM1864 host target gene. FOXJ1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FOXJ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXJ1 BINDING SITE, designated SEQ ID:7189, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61778] Another function of VGAM1864 is therefore inhibition of Forkhead Box J1 (FOXJ1, Accession NM\_001454). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXJ1. HYA22 (Accession NM\_005808) is another VGAM1864 host target gene. HYA22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by HYA22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HYA22 BINDING SITE, designated SEQ ID:12388, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61779] Another function of VGAM1864 is therefore inhibition of HYA22 (Accession NM\_005808). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HYA22. IDI2 (Accession NM\_033261) is another VGAM1864 host target gene. IDI2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IDI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IDI2 BINDING SITE, designated SEQ ID:27092, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61780] Another function of VGAM1864 is therefore inhibition of IDI2 (Accession NM\_033261). Accordingly, utilities of

VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IDI2. Potassium Inwardly-rectifying Channel, Subfamily J, Member 9 (KCNJ9, Accession NM\_004983) is another VGAM1864 host target gene. KCNJ9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNJ9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ9 BINDING SITE, designated SEQ ID:11431, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61781] Another function of VGAM1864 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 9 (KCNJ9, Accession NM\_004983). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ9. KIAA0513 (Accession NM\_014732) is another VGAM1864 host target gene. KIAA0513 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0513, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0513 BINDING SITE, designated SEQ ID:16363, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61782] Another function of VGAM1864 is therefore inhibition of KIAA0513 (Accession NM\_014732). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0513. KIAA0515 (Accession XM\_033380) is another VGAM1864 host target gene. KIAA0515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0515 BINDING SITE, designated SEQ ID:31925, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61783] Another function of VGAM1864 is therefore inhibition of KIAA0515 (Accession XM\_033380). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0515. KIAA0545 (Accession XM\_032278) is another VGAM1864 host target gene. KIAA0545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0545 BINDING SITE, designated SEQ ID:31637, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61784] Another function of VGAM1864 is therefore inhibition of KIAA0545 (Accession XM\_032278). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0545. KIAA0792 (Accession NM\_014698) is another VGAM1864 host target gene. KIAA0792 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0792, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0792 BINDING SITE, designated SEQ ID:16214, to the nucleotide sequence of VGAM1864 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4575.

[61785] Another function of VGAM1864 is therefore inhibition of KIAA0792 (Accession NM\_014698). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0792. KIAA0937 (Accession XM\_166213) is another VGAM1864 host target gene. KIAA0937 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0937 BINDING SITE, designated SEQ ID:44014, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61786] Another function of VGAM1864 is therefore inhibition of KIAA0937 (Accession XM\_166213). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0937. KIAA1126 (Accession XM\_050325) is another VGAM1864 host target gene. KIAA1126 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1126, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1126 BINDING SITE, designated SEQ ID:35606, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61787] Another function of VGAM1864 is therefore inhibition of KIAA1126 (Accession XM\_050325). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1126. KIAA1257 (Accession XM\_031577) is another VGAM1864 host target gene. KIAA1257 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1257 BINDING SITE, designated SEQ ID:31435, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61788] Another function of VGAM1864 is therefore inhibition of KIAA1257 (Accession XM\_031577). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with KIAA1257. KIAA1363 (Accession XM\_045056) is another VGAM1864 host target gene. KIAA1363 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1363, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1363 BINDING SITE, designated SEQ ID:34333, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61789] Another function of VGAM1864 is therefore inhibition of KIAA1363 (Accession XM\_045056). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1363. KIAA1377 (Accession XM\_040708) is another VGAM1864 host target gene. KIAA1377 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1377, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1377 BINDING SITE, designated SEQ ID:33360, to the

nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61790] Another function of VGAM1864 is therefore inhibition of KIAA1377 (Accession XM\_040708). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1377. KIAA1509 (Accession XM\_029353) is another VGAM1864 host target gene. KIAA1509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1509 BINDING SITE, designated SEQ ID:30874, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61791] Another function of VGAM1864 is therefore inhibition of KIAA1509 (Accession XM\_029353). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1509. KIAA1750 (Accession XM\_043067) is another VGAM1864 host target gene. KIAA1750 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1750 BINDING SITE, designated SEQ ID:33876, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61792] Another function of VGAM1864 is therefore inhibition of KIAA1750 (Accession XM\_043067). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1750. LIM and SH3 Protein 1 (LASP1, Accession NM\_006148) is another VGAM1864 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LASP1 BINDING SITE, designated SEQ ID:12800, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61793] Another function of VGAM1864 is therefore inhibition of

LIM and SH3 Protein 1 (LASP1, Accession NM\_006148). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. Leiomodlin 1 (smooth muscle) (LMOD1, Accession NM\_012134) is another VGAM1864 host target gene. LMOD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LMOD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMOD1 BINDING SITE, designated SEQ ID:14446, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61794] Another function of VGAM1864 is therefore inhibition of Leiomodlin 1 (smooth muscle) (LMOD1, Accession NM\_012134). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMOD1. Mitogen-activated Protein Kinase 13 (MAPK13, Accession NM\_002754) is another VGAM1864 host target gene. MAPK13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPK13, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK13 BINDING SITE, designated SEQ ID:8632, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61795] Another function of VGAM1864 is therefore inhibition of Mitogen-activated Protein Kinase 13 (MAPK13, Accession NM\_002754). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK13. MEP50 (Accession NM\_024102) is another VGAM1864 host target gene. MEP50 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEP50, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEP50 BINDING SITE, designated SEQ ID:23546, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61796] Another function of VGAM1864 is therefore inhibition of MEP50 (Accession NM\_024102). Accordingly, utilities of

VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEP50. PDEF (Accession NM\_012391) is another VGAM1864 host target gene. PDEF BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PDEF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDEF BINDING SITE, designated SEQ ID:14747, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61797] Another function of VGAM1864 is therefore inhibition of PDEF (Accession NM\_012391). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDEF. PHD Finger Protein 7 (PHF7, Accession NM\_016483) is another VGAM1864 host target gene. PHF7 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PHF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHF7 BINDING

SITE, designated SEQ ID:18581, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61798] Another function of VGAM1864 is therefore inhibition of PHD Finger Protein 7 (PHF7, Accession NM\_016483). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHF7. PPI5PIV (Accession NM\_019892) is another VGAM1864 host target gene. PPI5PIV BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPI5PIV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPI5PIV BINDING SITE, designated SEQ ID:21275, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61799] Another function of VGAM1864 is therefore inhibition of PPI5PIV (Accession NM\_019892). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPI5PIV. Protease, Serine, 25 (PRSS25, Accession NM\_013247) is another VGAM1864 host target gene. PRSS25 BINDING

SITE1 and PRSS25 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PRSS25, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRSS25 BINDING SITE1 and PRSS25 BINDING SITE2, designated SEQ ID:14908 and SEQ ID:29707 respectively, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61800] Another function of VGAM1864 is therefore inhibition of Protease, Serine, 25 (PRSS25, Accession NM\_013247). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRSS25. SARM (Accession NM\_015077) is another VGAM1864 host target gene. SARM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SARM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SARM BINDING SITE, designated SEQ ID:17454, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA,



also designated SEQ ID:4575.

[61801] Another function of VGAM1864 is therefore inhibition of SARM (Accession NM\_015077). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SARM. Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654) is another VGAM1864 host target gene. SDC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SDC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC3 BINDING SITE, designated SEQ ID:16080, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61802] Another function of VGAM1864 is therefore inhibition of Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC3. SKIP (Accession NM\_016532) is another VGAM1864 host target gene. SKIP BINDING SITE1 and SKIP BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

SKIP, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SKIP BINDING SITE1 and SKIP BINDING SITE2, designated SEQ ID:18596 and SEQ ID:28259 respectively, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61803] Another function of VGAM1864 is therefore inhibition of SKIP (Accession NM\_016532). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SKIP. TED (Accession NM\_015686) is another VGAM1864 host target gene. TED BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TED, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TED BINDING SITE, designated SEQ ID:17912, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61804] Another function of VGAM1864 is therefore inhibition of TED (Accession NM\_015686). Accordingly, utilities of

VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TED. Translocase of Outer Mitochondrial Membrane 70 Homolog A (yeast) (TOMM70A, Accession NM\_014820) is another VGAM1864 host target gene. TOMM70A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOMM70A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOMM70A BINDING SITE, designated SEQ ID:16792, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61805] Another function of VGAM1864 is therefore inhibition of Translocase of Outer Mitochondrial Membrane 70 Homolog A (yeast) (TOMM70A, Accession NM\_014820). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOMM70A. Zinc Finger Protein 313 (ZNF313, Accession NM\_018683) is another VGAM1864 host target gene. ZNF313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF313, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF313 BINDING SITE, designated SEQ ID:20753, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61806] Another function of VGAM1864 is therefore inhibition of Zinc Finger Protein 313 (ZNF313, Accession NM\_018683). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF313. LOC124044 (Accession XM\_071871) is another VGAM1864 host target gene. LOC124044 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124044, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124044 BINDING SITE, designated SEQ ID:37432, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61807] Another function of VGAM1864 is therefore inhibition of LOC124044 (Accession XM\_071871). Accordingly, utilities

of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124044. LOC124997 (Accession XM\_058886) is another VGAM1864 host target gene. LOC124997 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC124997, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124997 BINDING SITE, designated SEQ ID:36786, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61808] Another function of VGAM1864 is therefore inhibition of LOC124997 (Accession XM\_058886). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124997. LOC126006 (Accession XM\_058956) is another VGAM1864 host target gene. LOC126006 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC126006, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC126006 BINDING SITE, designated SEQ ID:36801, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61809] Another function of VGAM1864 is therefore inhibition of LOC126006 (Accession XM\_058956). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126006. LOC130813 (Accession XM\_065904) is another VGAM1864 host target gene. LOC130813 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130813 BINDING SITE, designated SEQ ID:37312, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61810] Another function of VGAM1864 is therefore inhibition of LOC130813 (Accession XM\_065904). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130813. LOC145371 (Accession XM\_085123) is another VGAM1864 host target gene. LOC145371 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145371 BINDING SITE, designated SEQ ID:37841, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61811] Another function of VGAM1864 is therefore inhibition of LOC145371 (Accession XM\_085123). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145371. LOC145438 (Accession XM\_096781) is another VGAM1864 host target gene. LOC145438 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145438 BINDING SITE, designated SEQ ID:40535, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61812] Another function of VGAM1864 is therefore inhibition of

LOC145438 (Accession XM\_096781). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145438. LOC146728 (Accession XM\_097074) is another VGAM1864 host target gene. LOC146728 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146728, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146728 BINDING SITE, designated SEQ ID:40724, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61813] Another function of VGAM1864 is therefore inhibition of LOC146728 (Accession XM\_097074). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146728. LOC148397 (Accession XM\_086171) is another VGAM1864 host target gene. LOC148397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC148397 BINDING SITE, designated SEQ ID:38526, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61814] Another function of VGAM1864 is therefore inhibition of LOC148397 (Accession XM\_086171). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148397. LOC149171 (Accession XM\_086450) is another VGAM1864 host target gene. LOC149171 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149171 BINDING SITE, designated SEQ ID:38667, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61815] Another function of VGAM1864 is therefore inhibition of LOC149171 (Accession XM\_086450). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149171. LOC149706 (Accession XM\_097718) is an-

other VGAM1864 host target gene. LOC149706 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149706 BINDING SITE, designated SEQ ID:41058, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61816] Another function of VGAM1864 is therefore inhibition of LOC149706 (Accession XM\_097718). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149706. LOC152805 (Accession XM\_087526) is another VGAM1864 host target gene. LOC152805 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152805, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152805 BINDING SITE, designated SEQ ID:39323, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61817] Another function of VGAM1864 is therefore inhibition of LOC152805 (Accession XM\_087526). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152805. LOC153577 (Accession XM\_098394) is another VGAM1864 host target gene. LOC153577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153577 BINDING SITE, designated SEQ ID:41646, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61818] Another function of VGAM1864 is therefore inhibition of LOC153577 (Accession XM\_098394). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153577. LOC157349 (Accession XM\_088298) is another VGAM1864 host target gene. LOC157349 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157349, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157349 BINDING SITE, designated SEQ ID:39598, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61819] Another function of VGAM1864 is therefore inhibition of LOC157349 (Accession XM\_088298). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157349. LOC157858 (Accession XM\_098833) is another VGAM1864 host target gene. LOC157858 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157858 BINDING SITE, designated SEQ ID:41865, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61820] Another function of VGAM1864 is therefore inhibition of LOC157858 (Accession XM\_098833). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC157858. LOC164382 (Accession XM\_104390) is another VGAM1864 host target gene. LOC164382 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164382 BINDING SITE, designated SEQ ID:42160, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61821] Another function of VGAM1864 is therefore inhibition of LOC164382 (Accession XM\_104390). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164382. LOC166042 (Accession XM\_093623) is another VGAM1864 host target gene. LOC166042 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC166042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166042 BINDING SITE, designated SEQ ID:40200, to the nucleotide sequence of VGAM1864 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4575.

[61822] Another function of VGAM1864 is therefore inhibition of LOC166042 (Accession XM\_093623). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166042. LOC196707 (Accession XM\_113616) is another VGAM1864 host target gene. LOC196707 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196707, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196707 BINDING SITE, designated SEQ ID:42297, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61823] Another function of VGAM1864 is therefore inhibition of LOC196707 (Accession XM\_113616). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196707. LOC199923 (Accession XM\_114057) is another VGAM1864 host target gene. LOC199923 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199923, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199923 BINDING SITE, designated SEQ ID:42670, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61824] Another function of VGAM1864 is therefore inhibition of LOC199923 (Accession XM\_114057). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199923. LOC200470 (Accession XM\_117235) is another VGAM1864 host target gene. LOC200470 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200470, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200470 BINDING SITE, designated SEQ ID:43306, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61825] Another function of VGAM1864 is therefore inhibition of LOC200470 (Accession XM\_117235). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC200470. LOC201617 (Accession XM\_117315) is another VGAM1864 host target gene. LOC201617 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201617 BINDING SITE, designated SEQ ID:43380, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61826] Another function of VGAM1864 is therefore inhibition of LOC201617 (Accession XM\_117315). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201617. LOC202126 (Accession XM\_117362) is another VGAM1864 host target gene. LOC202126 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202126, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202126 BINDING SITE, designated SEQ ID:43410, to



the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61827] Another function of VGAM1864 is therefore inhibition of LOC202126 (Accession XM\_117362). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202126. LOC203504 (Accession XM\_117550) is another VGAM1864 host target gene. LOC203504 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203504 BINDING SITE, designated SEQ ID:43572, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61828] Another function of VGAM1864 is therefore inhibition of LOC203504 (Accession XM\_117550). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203504. LOC204161 (Accession XM\_118480) is another VGAM1864 host target gene. LOC204161 BINDING SITE1 and LOC204161 BINDING SITE2 are HOST TARGET

binding sites found in untranslated regions of mRNA encoded by LOC204161, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204161 BINDING SITE1 and LOC204161 BINDING SITE2, designated SEQ ID:43579 and SEQ ID:43580 respectively, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61829] Another function of VGAM1864 is therefore inhibition of LOC204161 (Accession XM\_118480). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204161. LOC221463 (Accession XM\_166374) is another VGAM1864 host target gene. LOC221463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221463 BINDING SITE, designated SEQ ID:44199, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61830] Another function of VGAM1864 is therefore inhibition of LOC221463 (Accession XM\_166374). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221463. LOC221490 (Accession XM\_168084) is another VGAM1864 host target gene. LOC221490 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221490, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221490 BINDING SITE, designated SEQ ID:44987, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61831] Another function of VGAM1864 is therefore inhibition of LOC221490 (Accession XM\_168084). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221490. LOC253675 (Accession XM\_172990) is another VGAM1864 host target gene. LOC253675 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253675, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253675 BINDING SITE, designated SEQ ID:46263, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61832] Another function of VGAM1864 is therefore inhibition of LOC253675 (Accession XM\_172990). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253675. LOC253891 (Accession XM\_170485) is another VGAM1864 host target gene. LOC253891 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253891 BINDING SITE, designated SEQ ID:45323, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61833] Another function of VGAM1864 is therefore inhibition of LOC253891 (Accession XM\_170485). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC253891. LOC254228 (Accession XM\_171123) is another VGAM1864 host target gene. LOC254228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254228 BINDING SITE, designated SEQ ID:45920, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61834] Another function of VGAM1864 is therefore inhibition of LOC254228 (Accession XM\_171123). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254228. LOC255189 (Accession XM\_172929) is another VGAM1864 host target gene. LOC255189 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255189 BINDING SITE, designated SEQ ID:46194, to the nucleotide sequence of VGAM1864 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4575.

[61835] Another function of VGAM1864 is therefore inhibition of LOC255189 (Accession XM\_172929). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255189. LOC256502 (Accession XM\_170546) is another VGAM1864 host target gene. LOC256502 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256502, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256502 BINDING SITE, designated SEQ ID:45367, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61836] Another function of VGAM1864 is therefore inhibition of LOC256502 (Accession XM\_170546). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256502. LOC256581 (Accession XM\_174399) is another VGAM1864 host target gene. LOC256581 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256581, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256581 BINDING SITE, designated SEQ ID:46591, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61837] Another function of VGAM1864 is therefore inhibition of LOC256581 (Accession XM\_174399). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256581. LOC257447 (Accession XM\_096847) is another VGAM1864 host target gene. LOC257447 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257447 BINDING SITE, designated SEQ ID:40568, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61838] Another function of VGAM1864 is therefore inhibition of LOC257447 (Accession XM\_096847). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC257447. LOC51152 (Accession NM\_016181) is another VGAM1864 host target gene. LOC51152 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51152 BINDING SITE, designated SEQ ID:18284, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61839] Another function of VGAM1864 is therefore inhibition of LOC51152 (Accession NM\_016181). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51152. LOC90141 (Accession XM\_029373) is another VGAM1864 host target gene. LOC90141 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90141, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90141 BINDING SITE, designated SEQ ID:30880, to the



nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61840] Another function of VGAM1864 is therefore inhibition of LOC90141 (Accession XM\_029373). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90141. LOC92568 (Accession XM\_045852) is another VGAM1864 host target gene. LOC92568 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92568 BINDING SITE, designated SEQ ID:34579, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61841] Another function of VGAM1864 is therefore inhibition of LOC92568 (Accession XM\_045852). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92568. LOC93268 (Accession XM\_050158) is another VGAM1864 host target gene. LOC93268 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC93268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93268 BINDING SITE, designated SEQ ID:35588, to the nucleotide sequence of VGAM1864 RNA, herein designated VGAM RNA, also designated SEQ ID:4575.

[61842] Another function of VGAM1864 is therefore inhibition of LOC93268 (Accession XM\_050158). Accordingly, utilities of VGAM1864 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93268. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1865 (VGAM1865) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61843] VGAM1865 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1865 was detected is described hereinabove with reference to Figs. 1-8.

[61844] VGAM1865 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Callitrichine Herpesvirus 3. VGAM1865 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61845] VGAM1865 gene encodes a VGAM1865 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1865 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1865 precursor RNA is designated SEQ ID:1851, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1851 is located at position 122877 relative to the genome of Callitrichine Herpesvirus 3.

[61846] VGAM1865 precursor RNA folds onto itself, forming VGAM1865 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61847] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1865 folded precursor RNA into VGAM1865 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1865 RNA is designated SEQ ID:4576, and is provided hereinbelow with reference to the sequence listing part.

[61848] VGAM1865 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1865 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1865 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61849] VGAM1865 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1865 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1865 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1865 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1865 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61850] The complementary binding of VGAM1865 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1865 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1865

host target RNA into VGAM1865 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61851] It is appreciated that VGAM1865 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1865 host target genes. The mRNA of each one of this plurality of VGAM1865 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1865 RNA, herein designated VGAM RNA, and which when bound by VGAM1865 RNA causes inhibition of translation of respective one or more VGAM1865 host target proteins.

[61852] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1865 gene, herein designated VGAM GENE, on one or more VGAM1865 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61853] It is yet further appreciated that a function of VGAM1865 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1865 correlate with, and may be deduced from, the identity of the host target genes which VGAM1865 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61854] Nucleotide sequences of the VGAM1865 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1865 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1865 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1865 are further

described hereinbelow with reference to Table 1.

[61855] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1865 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1865 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61856] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1865 gene, herein designated VGAM is inhibition of expression of VGAM1865 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1865 correlate with, and may be deduced from, the identity of the target genes which VGAM1865 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61857] E2F Transcription Factor 3 (E2F3, Accession NM\_001949) is a VGAM1865 host target gene. E2F3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by E2F3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of E2F3 BINDING



SITE, designated SEQ ID:7665, to the nucleotide sequence of VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61858] A function of VGAM1865 is therefore inhibition of E2F Transcription Factor 3 (E2F3, Accession NM\_001949), a gene which binds dna and controls cell-cycle progression from g1 to s phase. Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E2F3. The function of E2F3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM475. Protein Tyrosine Phosphatase, Receptor Type, A (PTPRA, Accession NM\_002836) is another VGAM1865 host target gene. PTPRA BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PTPRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRA BINDING SITE, designated SEQ ID:8714, to the nucleotide sequence of VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61859] Another function of VGAM1865 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, A (PTPRA, Accession NM\_002836), a gene which is the human homolog of the murine PTPase. Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRA. The function of PTPRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1205.SH3-domain GRB2-like 1 (SH3GL1, Accession NM\_003025) is another VGAM1865 host target gene. SH3GL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3GL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3GL1 BINDING SITE, designated SEQ ID:8964, to the nucleotide sequence of VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61860] Another function of VGAM1865 is therefore inhibition of SH3-domain GRB2-like 1 (SH3GL1, Accession NM\_003025). Accordingly, utilities of VGAM1865 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3GL1. Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM\_003038) is another VGAM1865 host target gene. SLC1A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A4 BINDING SITE, designated SEQ ID:8993, to the nucleotide sequence of VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61861] Another function of VGAM1865 is therefore inhibition of Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM\_003038), a gene which transports alanine, serine, cysteine, and threonine. exhibits sodium dependence. Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A4. The function of SLC1A4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM859.Solute Carrier Family 21 (organic anion transporter), Member 9 (SLC21A9, Accession NM\_007256) is another VGAM1865 host target gene. SLC21A9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC21A9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC21A9 BINDING SITE, designated SEQ ID:14125, to the nucleotide sequence of VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61862] Another function of VGAM1865 is therefore inhibition of Solute Carrier Family 21 (organic anion transporter), Member 9 (SLC21A9, Accession NM\_007256), a gene which is Moderately similar to SLC21A2 prostaglandin transporter. Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC21A9. The function of SLC21A9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM894.Tumor Necrosis Factor, Alpha-induced Protein

2 (TNFAIP2, Accession NM\_006291) is another VGAM1865 host target gene. TNFAIP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TNFAIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFAIP2 BINDING SITE, designated SEQ ID:12982, to the nucleotide sequence of VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61863] Another function of VGAM1865 is therefore inhibition of Tumor Necrosis Factor, Alpha-induced Protein 2 (TNFAIP2, Accession NM\_006291). Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFAIP2. C1q and Tumor Necrosis Factor Related Protein 7 (C1QTNF7, Accession NM\_031911) is another VGAM1865 host target gene. C1QTNF7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1QTNF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QTNF7 BINDING SITE,

designated SEQ ID:25661, to the nucleotide sequence of VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61864] Another function of VGAM1865 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 7 (C1QTNF7, Accession NM\_031911). Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF7. KIAA1979 (Accession XM\_113984) is another VGAM1865 host target gene. KIAA1979 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1979 BINDING SITE, designated SEQ ID:42591, to the nucleotide sequence of VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61865] Another function of VGAM1865 is therefore inhibition of KIAA1979 (Accession XM\_113984). Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1979. STAF65(gamma) (Accession NM\_014860) is

another VGAM1865 host target gene. STAF65(gamma) BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STAF65(gamma), corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAF65(gamma) BINDING SITE, designated SEQ ID:16926, to the nucleotide sequence of VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61866] Another function of VGAM1865 is therefore inhibition of STAF65(gamma) (Accession NM\_014860). Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAF65(gamma). LOC146856 (Accession XM\_096086) is another VGAM1865 host target gene. LOC146856 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC146856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146856 BINDING SITE, designated SEQ ID:40298, to the nucleotide sequence of

VGAM1865 RNA, herein designated VGAM RNA, also designated SEQ ID:4576.

[61867] Another function of VGAM1865 is therefore inhibition of LOC146856 (Accession XM\_096086). Accordingly, utilities of VGAM1865 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146856. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1866 (VGAM1866) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61868] VGAM1866 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1866 was detected is described hereinabove with reference to Figs. 1–8.

[61869] VGAM1866 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM1866 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61870] VGAM1866 gene encodes a VGAM1866 precursor RNA,



herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1866 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1866 precursor RNA is designated SEQ ID:1852, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1852 is located at position 121344 relative to the genome of Callitrichine Herpesvirus 3.

[61871] VGAM1866 precursor RNA folds onto itself, forming VGAM1866 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61872] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1866 folded precursor RNA into VGAM1866 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1866 RNA is designated SEQ ID:4577, and is provided hereinbelow with reference to the sequence listing part.

[61873] VGAM1866 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1866 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1866 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61874] VGAM1866 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1866 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1866 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1866 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1866 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61875] The complementary binding of VGAM1866 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1866 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1866 host target RNA into VGAM1866 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61876] It is appreciated that VGAM1866 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1866 host target genes. The mRNA of each one of this plurality of VGAM1866 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1866 RNA, herein designated VGAM RNA, and which when bound by VGAM1866 RNA causes inhibition of translation of respective one or more VGAM1866 host target proteins.

[61877] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1866 gene, herein designated VGAM GENE, on one or more VGAM1866 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[61878] It is yet further appreciated that a function of VGAM1866 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1866 correlate with, and may be deduced from, the identity of the host target genes which VGAM1866 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61879] Nucleotide sequences of the VGAM1866 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1866 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1866 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1866 are further described hereinbelow with reference to Table 1.

[61880] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1866 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1866 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61881] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1866 gene, herein designated VGAM is inhibition of expression of VGAM1866 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1866 correlate with, and may be deduced from, the identity of the target genes which VGAM1866 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61882] BRF1 Homolog, Subunit of RNA Polymerase III Transcription Initiation Factor IIIB (*S. cerevisiae*) (BRF1, Accession NM\_001519) is a VGAM1866 host target gene. BRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRF1 BINDING SITE, designated SEQ ID:7254, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61883] A function of VGAM1866 is therefore inhibition of BRF1

Homolog, Subunit of RNA Polymerase III Transcription Initiation Factor IIIB (*S. cerevisiae*) (BRF1, Accession NM\_001519), a gene which is a general activator of RNA polymerase III. Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRF1. The function of BRF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. HERV-H LTR-associating 1 (HHLA1, Accession NM\_005712) is another VGAM1866 host target gene. HHLA1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HHLA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HHLA1 BINDING SITE, designated SEQ ID:12264, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61884] Another function of VGAM1866 is therefore inhibition of HERV-H LTR-associating 1 (HHLA1, Accession NM\_005712), a gene which has unknown function and with low similarity to a region of *S. cerevisiae* WSC4. Ac-

cordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HHLA1. The function of HHLA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM158. Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM\_002507) is another VGAM1866 host target gene. NGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGFR BINDING SITE, designated SEQ ID:8333, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61885] Another function of VGAM1866 is therefore inhibition of Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM\_002507), a gene which can mediate cell survival as well as cell death of neural cells. Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGFR. The function of NGFR and its asso-



ciation with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM212. Protein Tyrosine Phosphatase, Non-receptor Type 18 (brain-derived) (PTPN18, Accession NM\_014369) is another VGAM1866 host target gene. PTPN18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPN18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPN18 BINDING SITE, designated SEQ ID:15702, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61886] Another function of VGAM1866 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type 18 (brain-derived) (PTPN18, Accession NM\_014369). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPN18. Vitamin D (1,25-dihydroxyvitamin D3) Receptor (VDR, Accession NM\_000376) is another VGAM1866 host target gene. VDR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by VDR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VDR BINDING SITE, designated SEQ ID:5942, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61887] Another function of VGAM1866 is therefore inhibition of Vitamin D (1,25- dihydroxyvitamin D3) Receptor (VDR, Accession NM\_000376). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VDR. A2BP1 (Accession NM\_018723) is another VGAM1866 host target gene. A2BP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by A2BP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of A2BP1 BINDING SITE, designated SEQ ID:20802, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61888] Another function of VGAM1866 is therefore inhibition of

A2BP1 (Accession NM\_018723). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with A2BP1. Bromodomain Containing 4 (BRD4, Accession NM\_058243) is another VGAM1866 host target gene. BRD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRD4 BINDING SITE, designated SEQ ID:27773, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61889] Another function of VGAM1866 is therefore inhibition of Bromodomain Containing 4 (BRD4, Accession NM\_058243). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRD4. DKFZP564B1162 (Accession NM\_031305) is another VGAM1866 host target gene. DKFZP564B1162 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564B1162, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564B1162 BINDING SITE, designated SEQ ID:25336, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61890] Another function of VGAM1866 is therefore inhibition of DKFZP564B1162 (Accession NM\_031305). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564B1162. KIAA1607 (Accession XM\_033379) is another VGAM1866 host target gene. KIAA1607 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1607, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1607 BINDING SITE, designated SEQ ID:31913, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61891] Another function of VGAM1866 is therefore inhibition of KIAA1607 (Accession XM\_033379). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1607. KIAA1987 (Accession XM\_113870) is another VGAM1866 host target gene. KIAA1987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1987 BINDING SITE, designated SEQ ID:42491, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61892] Another function of VGAM1866 is therefore inhibition of KIAA1987 (Accession XM\_113870). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1987. LOC116113 (Accession XM\_166413) is another VGAM1866 host target gene. LOC116113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116113 BINDING SITE, designated SEQ ID:44282, to the nucleotide sequence of VGAM1866 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4577.

[61893] Another function of VGAM1866 is therefore inhibition of LOC116113 (Accession XM\_166413). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116113. LOC162333 (Accession XM\_102591) is another VGAM1866 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42132, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61894] Another function of VGAM1866 is therefore inhibition of LOC162333 (Accession XM\_102591). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC221495 (Accession XM\_168136) is another VGAM1866 host target gene. LOC221495 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221495, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221495 BINDING SITE, designated SEQ ID:45055, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61895] Another function of VGAM1866 is therefore inhibition of LOC221495 (Accession XM\_168136). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221495. LOC257479 (Accession XM\_171548) is another VGAM1866 host target gene. LOC257479 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257479 BINDING SITE, designated SEQ ID:46053, to the nucleotide sequence of VGAM1866 RNA, herein designated VGAM RNA, also designated SEQ ID:4577.

[61896] Another function of VGAM1866 is therefore inhibition of LOC257479 (Accession XM\_171548). Accordingly, utilities of VGAM1866 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC257479. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1867 (VGAM1867) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61897] VGAM1867 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1867 was detected is described hereinabove with reference to Figs. 1–8.

[61898] VGAM1867 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM1867 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61899] VGAM1867 gene encodes a VGAM1867 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1867 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1867 precursor RNA is desig-



nated SEQ ID:1853, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1853 is located at position 121561 relative to the genome of Callitrichine Herpesvirus 3.

- [61900] VGAM1867 precursor RNA folds onto itself, forming VGAM1867 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [61901] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1867 folded precursor RNA into VGAM1867 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1867 RNA is designated SEQ ID:4578, and is provided hereinbelow with reference to the sequence

listing part.

[61902] VGAM1867 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1867 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1867 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61903] VGAM1867 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1867 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1867 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1867 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1867 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61904] The complementary binding of VGAM1867 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1867 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1867 host target RNA into VGAM1867 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61905] It is appreciated that VGAM1867 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1867 host target genes. The mRNA of each one of this plurality of VGAM1867 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1867 RNA, herein designated VGAM

RNA, and which when bound by VGAM1867 RNA causes inhibition of translation of respective one or more VGAM1867 host target proteins.

[61906] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1867 gene, herein designated VGAM GENE, on one or more VGAM1867 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61907] It is yet further appreciated that a function of VGAM1867 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1867 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1867 correlate with, and may be deduced from, the identity of the host target genes which VGAM1867 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61908] Nucleotide sequences of the VGAM1867 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1867 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1867 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1867 are further described hereinbelow with reference to Table 1.

[61909] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1867 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1867 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61910] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1867 gene, herein designated VGAM is

inhibition of expression of VGAM1867 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1867 correlate with, and may be deduced from, the identity of the target genes which VGAM1867 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61911] Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III) (AGL, Accession NM\_000646) is a VGAM1867 host target gene. AGL BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AGL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGL BINDING SITE, designated SEQ ID:6301, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61912] A function of VGAM1867 is therefore inhibition of Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III) (AGL, Accession NM\_000646). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGL.

Ras Homolog Gene Family, Member C (ARHC, Accession NM\_005167) is another VGAM1867 host target gene. ARHC BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ARHC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHC BINDING SITE, designated SEQ ID:11661, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61913] Another function of VGAM1867 is therefore inhibition of Ras Homolog Gene Family, Member C (ARHC, Accession NM\_005167), a gene which remodels of the actin cytoskeleton during cell morphogenesis and motility. Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHC. The function of ARHC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM885.Deleted In Azoospermia-like (DAZL, Accession XM\_042839) is another VGAM1867 host target gene. DAZL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by DAZL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAZL BINDING SITE, designated SEQ ID:33797, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61914] Another function of VGAM1867 is therefore inhibition of Deleted In Azoospermia-like (DAZL, Accession XM\_042839), a gene which may be essential for gametogenesis. Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAZL. The function of DAZL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206.FBJ Murine Osteosarcoma Viral Oncogene Homolog B (FOSB, Accession NM\_006732) is another VGAM1867 host target gene. FOSB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-



quences of FOSB BINDING SITE, designated SEQ ID:13579, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61915] Another function of VGAM1867 is therefore inhibition of FBJ Murine Osteosarcoma Viral Oncogene Homolog B (FOSB, Accession NM\_006732), a gene which interacts with jun proteins enhancing their dna binding activity. Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOSB. The function of FOSB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM747.3-hydroxy-3-methylglutaryl-Coenzyme A Reductase (HMGCR, Accession NM\_000859) is another VGAM1867 host target gene. HMGCR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGCR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGCR BINDING SITE, designated SEQ ID:6521, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM

RNA, also designated SEQ ID:4578.

[61916] Another function of VGAM1867 is therefore inhibition of 3-hydroxy-3-methylglutaryl-Coenzyme A Reductase (HMGCR, Accession NM\_000859), a gene which is involved in the control of cholesterol biosynthesis and is the rate-limiting enzyme of sterol biosynthesis. Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGCR. The function of HMGCR has been established by previous studies. Although catalyzing a rate-limiting step in cholesterol biosynthesis (see OMIM Ref. No. 143890) is the best known role of HMG-CoA reductase, the enzyme also participates in the production of a wide variety of other compounds. Some clinical benefits attributed to inhibitors of HMG-CoA reductase appear to be independent of any serum cholesterol-lowering effect. Van Doren et al. (1998) described a new cholesterol-independent role for the enzyme, in regulating a developmental process, primordial germ cell migration. They showed that in *Drosophila* this enzyme is highly expressed in the somatic gonad and that it is necessary for primordial germ cells to migrate to this tissue. Misexpression of HMG-CoA reductase was sufficient to attract pri-

mordial germ cells to tissues other than the gonadal mesoderm. Van Doren et al. (1998) concluded that the regulated expression of HMG-CoA reductase has a critical developmental function in providing spatial information to guide migrating primordial germ cells. Istvan and Deisenhofer (2001) determined structures of the catalytic portion of human HMG-CoA reductase complexed with 6 different statins. The statins occupy a portion of the binding site of HMG-CoA, thus blocking access of this substrate to the active site. Near the carboxyl terminus of HMG-CoA reductase, several catalytically relevant residues are disordered in the enzyme-statin complexes. If these residues were not flexible, they would sterically hinder statin binding.

[61917] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[61918] Van Doren, M.; Broihier, H. T.; Moore, L. A.; Lehmann, R. : HMG-CoA reductase guides migrating primordial germ cells. *Nature* 396: 466-469, 1998. ; and

[61919] Istvan, E. S.; Deisenhofer, J. : Structural mechanism for statin inhibition of HMG-CoA reductase. *Science* 292: 1160-1164, 2001.

[61920] Further studies establishing the function and utilities of HMGCR are found in John Hopkins OMIM database record ID 142910, and in cited publications numbered 11712–11713, 359 and 3614–3618 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Lecithin Retinol Acyltransferase (phosphatidylcholine--retinol O-acyltransferase) (LRAT, Accession XM\_011181) is another VGAM1867 host target gene. LRAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRAT BINDING SITE, designated SEQ ID:30181, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61921] Another function of VGAM1867 is therefore inhibition of Lecithin Retinol Acyltransferase (phosphatidylcholine--retinol O-acyltransferase) (LRAT, Accession XM\_011181). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRAT. Myotubularin Related Protein 8 (MTMR8, Accession

NM\_015458) is another VGAM1867 host target gene.

MTMR8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTMR8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR8 BINDING SITE, designated SEQ ID:17742, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61922] Another function of VGAM1867 is therefore inhibition of Myotubularin Related Protein 8 (MTMR8, Accession NM\_015458), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTMR8. The function of MTMR8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM379. Neurocalcin Delta (NCALD, Accession NM\_032041) is another VGAM1867 host target gene. NCALD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

NCALD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCALD BINDING SITE, designated SEQ ID:25742, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61923] Another function of VGAM1867 is therefore inhibition of Neurocalcin Delta (NCALD, Accession NM\_032041). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCALD. PACE (Accession NM\_002569) is another VGAM1867 host target gene. PACE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACE BINDING SITE, designated SEQ ID:8421, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61924] Another function of VGAM1867 is therefore inhibition of PACE (Accession NM\_002569), a gene which processes

pro-parathyroid hormone, pro-transforming growth factor beta. Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACE. The function of PACE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM151. Protein Tyrosine Phosphatase, Non-receptor Type 7 (PTPN7, Accession NM\_002832) is another VGAM1867 host target gene. PTPN7 BINDING SITE1 through PTPN7 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPN7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPN7 BINDING SITE1 through PTPN7 BINDING SITE3, designated SEQ ID:8708, SEQ ID:27886 and SEQ ID:27889 respectively, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61925] Another function of VGAM1867 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type 7 (PTPN7, Accession NM\_002832). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PTPN7. DKFZp434F054 (Accession NM\_032259) is another VGAM1867 host target gene. DKFZp434F054 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp434F054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434F054 BINDING SITE, designated SEQ ID:26002, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61926] Another function of VGAM1867 is therefore inhibition of DKFZp434F054 (Accession NM\_032259). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434F054. FACTP140 (Accession NM\_007192) is another VGAM1867 host target gene. FACTP140 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FACTP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of



FACTP140 BINDING SITE, designated SEQ ID:14045, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61927] Another function of VGAM1867 is therefore inhibition of FACTP140 (Accession NM\_007192). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FACTP140. FLJ11099 (Accession NM\_018320) is another VGAM1867 host target gene. FLJ11099 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11099, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11099 BINDING SITE, designated SEQ ID:20312, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61928] Another function of VGAM1867 is therefore inhibition of FLJ11099 (Accession NM\_018320). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11099. FLJ20436 (Accession NM\_017822) is another VGAM1867 host target gene. FLJ20436 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20436, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20436 BINDING SITE, designated SEQ ID:19474, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61929] Another function of VGAM1867 is therefore inhibition of FLJ20436 (Accession NM\_017822). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20436. FLJ21977 (Accession NM\_032213) is another VGAM1867 host target gene. FLJ21977 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21977 BINDING SITE, designated SEQ ID:25938, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61930] Another function of VGAM1867 is therefore inhibition of

FLJ21977 (Accession NM\_032213). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21977. HCA127 (Accession NM\_018684) is another VGAM1867 host target gene. HCA127 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCA127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA127 BINDING SITE, designated SEQ ID:20758, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61931] Another function of VGAM1867 is therefore inhibition of HCA127 (Accession NM\_018684). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCA127. KIAA0493 (Accession XM\_034717) is another VGAM1867 host target gene. KIAA0493 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0493 BINDING SITE, designated SEQ ID:32141, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61932] Another function of VGAM1867 is therefore inhibition of KIAA0493 (Accession XM\_034717). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0493. KIAA0618 (Accession NM\_014833) is another VGAM1867 host target gene. KIAA0618 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0618 BINDING SITE, designated SEQ ID:16838, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61933] Another function of VGAM1867 is therefore inhibition of KIAA0618 (Accession NM\_014833). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0618. MGC20235 (Accession NM\_145041) is another

VGAM1867 host target gene. MGC20235 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC20235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20235 BINDING SITE, designated SEQ ID:29667, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61934] Another function of VGAM1867 is therefore inhibition of MGC20235 (Accession NM\_145041). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20235. MGC23280 (Accession NM\_144683) is another VGAM1867 host target gene. MGC23280 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC23280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC23280 BINDING SITE, designated SEQ ID:29500, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61935] Another function of VGAM1867 is therefore inhibition of MGC23280 (Accession NM\_144683). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC23280. MGC4771 (Accession NM\_032668) is another VGAM1867 host target gene. MGC4771 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4771, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4771 BINDING SITE, designated SEQ ID:26395, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61936] Another function of VGAM1867 is therefore inhibition of MGC4771 (Accession NM\_032668). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4771. MGC5149 (Accession XM\_051200) is another VGAM1867 host target gene. MGC5149 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC5149, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5149 BINDING SITE, designated SEQ ID:35781, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61937] Another function of VGAM1867 is therefore inhibition of MGC5149 (Accession XM\_051200). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5149. poly(rC) Binding Protein 4 (PCBP4, Accession NM\_033008) is another VGAM1867 host target gene. PCBP4 BINDING SITE1 through PCBP4 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCBP4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCBP4 BINDING SITE1 through PCBP4 BINDING SITE3, designated SEQ ID:26893, SEQ ID:26895 and SEQ ID:21677 respectively, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61938] Another function of VGAM1867 is therefore inhibition of poly(rC) Binding Protein 4 (PCBP4, Accession NM\_033008).

Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCBP4. LOC129566 (Accession XM\_065294) is another VGAM1867 host target gene. LOC129566 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC129566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129566 BINDING SITE, designated SEQ ID:37278, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61939] Another function of VGAM1867 is therefore inhibition of LOC129566 (Accession XM\_065294). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129566. LOC130595 (Accession XM\_065793) is another VGAM1867 host target gene. LOC130595 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC130595, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC130595 BINDING SITE, designated SEQ ID:37298, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61940] Another function of VGAM1867 is therefore inhibition of LOC130595 (Accession XM\_065793). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130595. LOC143286 (Accession XM\_096412) is another VGAM1867 host target gene. LOC143286 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143286 BINDING SITE, designated SEQ ID:40352, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61941] Another function of VGAM1867 is therefore inhibition of LOC143286 (Accession XM\_096412). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143286. LOC144438 (Accession XM\_084860) is an-

other VGAM1867 host target gene. LOC144438 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144438 BINDING SITE, designated SEQ ID:37733, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61942] Another function of VGAM1867 is therefore inhibition of LOC144438 (Accession XM\_084860). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144438. LOC147077 (Accession XM\_085699) is another VGAM1867 host target gene. LOC147077 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147077 BINDING SITE, designated SEQ ID:38289, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61943] Another function of VGAM1867 is therefore inhibition of LOC147077 (Accession XM\_085699). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147077. LOC152765 (Accession XM\_087519) is another VGAM1867 host target gene. LOC152765 BINDING SITE1 and LOC152765 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC152765, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152765 BINDING SITE1 and LOC152765 BINDING SITE2, designated SEQ ID:39309 and SEQ ID:39310 respectively, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61944] Another function of VGAM1867 is therefore inhibition of LOC152765 (Accession XM\_087519). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152765. LOC153577 (Accession XM\_098394) is another VGAM1867 host target gene. LOC153577 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC153577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153577 BINDING SITE, designated SEQ ID:41642, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61945] Another function of VGAM1867 is therefore inhibition of LOC153577 (Accession XM\_098394). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153577. LOC90936 (Accession XM\_034953) is another VGAM1867 host target gene. LOC90936 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90936 BINDING SITE, designated SEQ ID:32189, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61946] Another function of VGAM1867 is therefore inhibition of LOC90936 (Accession XM\_034953). Accordingly, utilities

of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90936. LOC92218 (Accession XM\_043647) is another VGAM1867 host target gene. LOC92218 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92218 BINDING SITE, designated SEQ ID:33986, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61947] Another function of VGAM1867 is therefore inhibition of LOC92218 (Accession XM\_043647). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92218. LOC92305 (Accession NM\_138385) is another VGAM1867 host target gene. LOC92305 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC92305 BINDING SITE, designated SEQ ID:28757, to the nucleotide sequence of VGAM1867 RNA, herein designated VGAM RNA, also designated SEQ ID:4578.

[61948] Another function of VGAM1867 is therefore inhibition of LOC92305 (Accession NM\_138385). Accordingly, utilities of VGAM1867 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92305. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1868 (VGAM1868) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61949] VGAM1868 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1868 was detected is described hereinabove with reference to Figs. 1–8.

[61950] VGAM1868 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM1868 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61951] VGAM1868 gene encodes a VGAM1868 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1868 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1868 precursor RNA is designated SEQ ID:1854, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1854 is located at position 119545 relative to the genome of Callitrichine Herpesvirus 3.

[61952] VGAM1868 precursor RNA folds onto itself, forming VGAM1868 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[61953] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1868 folded precursor RNA into VGAM1868 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1868 RNA is designated SEQ ID:4579, and is provided hereinbelow with reference to the sequence listing part.

[61954] VGAM1868 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1868 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1868 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61955] VGAM1868 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1868 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1868 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-



illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1868 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1868 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61956] The complementary binding of VGAM1868 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1868 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1868 host target RNA into VGAM1868 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61957] It is appreciated that VGAM1868 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1868 host target genes. The mRNA of each one of this plurality of VGAM1868 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1868 RNA, herein designated VGAM RNA, and which when bound by VGAM1868 RNA causes inhibition of translation of respective one or more VGAM1868 host target proteins.

[61958] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1868 gene, herein designated VGAM GENE, on one or more VGAM1868 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[61959] It is yet further appreciated that a function of VGAM1868 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1868 correlate with, and may be deduced from, the identity of the host target genes which VGAM1868 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61960] Nucleotide sequences of the VGAM1868 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1868 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1868 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1868 are further described hereinbelow with reference to Table 1.

[61961] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1868 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1868 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61962] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1868 gene, herein designated VGAM is inhibition of expression of VGAM1868 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1868 correlate with, and may be deduced from, the identity of the target genes which VGAM1868 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61963] V-akt Murine Thymoma Viral Oncogene Homolog 1 (AKT1, Accession NM\_005163) is a VGAM1868 host target gene. AKT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKT1 BINDING SITE, designated SEQ ID:11653, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61964] A function of VGAM1868 is therefore inhibition of V-akt

Murine Thymoma Viral Oncogene Homolog 1 (AKT1, Accession NM\_005163), a gene which Serine-threonine protein kinase. Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKT1. The function of AKT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM188.Estrogen-related Receptor Gamma (ESRRG, Accession XM\_039053) is another VGAM1868 host target gene. ESRRG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESRRG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESRRG BINDING SITE, designated SEQ ID:33000, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61965] Another function of VGAM1868 is therefore inhibition of Estrogen-related Receptor Gamma (ESRRG, Accession XM\_039053), a gene which Estrogen-related receptor gamma. Accordingly, utilities of VGAM1868 include diag-

nosis, prevention and treatment of diseases and clinical conditions associated with ESRRG. The function of ESRRG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM359. Protocadherin Beta 9 (PCDHB9, Accession NM\_019119) is another VGAM1868 host target gene. PCDHB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB9 BINDING SITE, designated SEQ ID:21204, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61966] Another function of VGAM1868 is therefore inhibition of Protocadherin Beta 9 (PCDHB9, Accession NM\_019119), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHB9. The function of PCDHB9 and its association with various diseases and

clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.Sialyltransferase 8E (alpha-2, 8-polysialyltransferase) (SIAT8E, Accession XM\_008705) is another VGAM1868 host target gene. SIAT8E BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SIAT8E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT8E BINDING SITE, designated SEQ ID:30089, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61967] Another function of VGAM1868 is therefore inhibition of Sialyltransferase 8E (alpha-2, 8-polysialyltransferase) (SIAT8E, Accession XM\_008705). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT8E. TNF Receptor-associated Factor 1 (TRAF1, Accession NM\_005658) is another VGAM1868 host target gene. TRAF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRAF1, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAF1 BINDING SITE, designated SEQ ID:12197, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61968] Another function of VGAM1868 is therefore inhibition of TNF Receptor-associated Factor 1 (TRAF1, Accession NM\_005658), a gene which signal transducer associated with the cytoplasmic domain of the 75 kda tumor necrosis factor receptor (tnf-r2). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF1. The function of TRAF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM250.DKFZP434G1411 (Accession XM\_166383) is another VGAM1868 host target gene. DKFZP434G1411 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434G1411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-



cleotide sequences of DKFZP434G1411 BINDING SITE, designated SEQ ID:44230, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61969] Another function of VGAM1868 is therefore inhibition of DKFZP434G1411 (Accession XM\_166383). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434G1411. FLJ10956 (Accession NM\_018283) is another VGAM1868 host target gene. FLJ10956 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10956, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10956 BINDING SITE, designated SEQ ID:20276, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61970] Another function of VGAM1868 is therefore inhibition of FLJ10956 (Accession NM\_018283). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10956. FLJ12787 (Accession NM\_032175) is another

VGAM1868 host target gene. FLJ12787 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12787, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12787 BINDING SITE, designated SEQ ID:25889, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61971] Another function of VGAM1868 is therefore inhibition of FLJ12787 (Accession NM\_032175). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12787. Oxysterol Binding Protein-like 11 (OSBPL11, Accession NM\_022776) is another VGAM1868 host target gene. OSBPL11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL11 BINDING SITE, designated SEQ ID:23045, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ

ID:4579.

[61972] Another function of VGAM1868 is therefore inhibition of Oxysterol Binding Protein-like 11 (OSBPL11, Accession NM\_022776). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL11. PSR (Accession XM\_036784) is another VGAM1868 host target gene. PSR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSR BINDING SITE, designated SEQ ID:32495, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61973] Another function of VGAM1868 is therefore inhibition of PSR (Accession XM\_036784). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSR. RA-GEF-2 (Accession NM\_016340) is another VGAM1868 host target gene. RA-GEF-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RA-GEF-2, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RA-GEF-2 BINDING SITE, designated SEQ ID:18460, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61974] Another function of VGAM1868 is therefore inhibition of RA-GEF-2 (Accession NM\_016340). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RA-GEF-2. LOC149401 (Accession XM\_086511) is another VGAM1868 host target gene. LOC149401 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149401 BINDING SITE, designated SEQ ID:38735, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61975] Another function of VGAM1868 is therefore inhibition of LOC149401 (Accession XM\_086511). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC149401. LOC157860 (Accession XM\_098832) is another VGAM1868 host target gene. LOC157860 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC157860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157860 BINDING SITE, designated SEQ ID:41860, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61976] Another function of VGAM1868 is therefore inhibition of LOC157860 (Accession XM\_098832). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157860. LOC158927 (Accession XM\_099004) is another VGAM1868 host target gene. LOC158927 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC158927, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158927 BINDING SITE, designated SEQ ID:42040, to

the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61977] Another function of VGAM1868 is therefore inhibition of LOC158927 (Accession XM\_099004). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158927. LOC165552 (Accession XM\_092666) is another VGAM1868 host target gene. LOC165552 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC165552, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165552 BINDING SITE, designated SEQ ID:40132, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61978] Another function of VGAM1868 is therefore inhibition of LOC165552 (Accession XM\_092666). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165552. LOC92370 (Accession XM\_044665) is another VGAM1868 host target gene. LOC92370 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC92370, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92370 BINDING SITE, designated SEQ ID:34258, to the nucleotide sequence of VGAM1868 RNA, herein designated VGAM RNA, also designated SEQ ID:4579.

[61979] Another function of VGAM1868 is therefore inhibition of LOC92370 (Accession XM\_044665). Accordingly, utilities of VGAM1868 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92370. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1869 (VGAM1869) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[61980] VGAM1869 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1869 was detected is described hereinabove with reference to Figs. 1-8.

[61981] VGAM1869 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Equine Herpesvirus 2. VGAM1869 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[61982] VGAM1869 gene encodes a VGAM1869 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1869 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1869 precursor RNA is designated SEQ ID:1855, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1855 is located at position 125161 relative to the genome of Equine Herpesvirus 2.

[61983] VGAM1869 precursor RNA folds onto itself, forming VGAM1869 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.



[61984] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1869 folded precursor RNA into VGAM1869 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1869 RNA is designated SEQ ID:4580, and is provided hereinbelow with reference to the sequence listing part.

[61985] VGAM1869 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1869 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1869 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[61986] VGAM1869 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1869 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1869 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1869 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1869 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[61987] The complementary binding of VGAM1869 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1869 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1869

host target RNA into VGAM1869 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[61988] It is appreciated that VGAM1869 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1869 host target genes. The mRNA of each one of this plurality of VGAM1869 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1869 RNA, herein designated VGAM RNA, and which when bound by VGAM1869 RNA causes inhibition of translation of respective one or more VGAM1869 host target proteins.

[61989] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1869 gene, herein designated VGAM GENE, on one or more VGAM1869 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[61990] It is yet further appreciated that a function of VGAM1869 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1869 correlate with, and may be deduced from, the identity of the host target genes which VGAM1869 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[61991] Nucleotide sequences of the VGAM1869 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1869 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1869 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1869 are further

described hereinbelow with reference to Table 1.

[61992] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1869 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1869 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[61993] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1869 gene, herein designated VGAM is inhibition of expression of VGAM1869 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1869 correlate with, and may be deduced from, the identity of the target genes which VGAM1869 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[61994] CDP-diacylglycerol Synthase (phosphatidate cytidylyl-transferase) 2 (CDS2, Accession NM\_003818) is a VGAM1869 host target gene. CDS2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of CDS2 BINDING SITE, designated SEQ ID:9908, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[61995] A function of VGAM1869 is therefore inhibition of CDP-diacylglycerol Synthase (phosphatidate cytidylyltransferase) 2 (CDS2, Accession NM\_003818), a gene which is a key regulator of the amount of PIP2 available for signaling. Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDS2. The function of CDS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM900. Dysferlin, Limb Girdle Muscular Dystrophy 2B (autosomal recessive) (DYSF, Accession NM\_003494) is another VGAM1869 host target gene. DYSF BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DYSF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYSF BINDING SITE, designated SEQ ID:9585, to the nucleotide sequence of VGAM1869 RNA, herein

designated VGAM RNA, also designated SEQ ID:4580.

[61996] Another function of VGAM1869 is therefore inhibition of Dysferlin, Limb Girdle Muscular Dystrophy 2B (autosomal recessive) (DYSF, Accession NM\_003494), a gene which is highly expressed in skeletal muscle. Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYSF. The function of DYSF has been established by previous studies. The limb-girdle muscular dystrophies are a genetically heterogeneous group of inherited progressive muscular disorders that affect mainly the proximal musculature, with evidence for at least 3 autosomal dominant and 8 autosomal recessive loci. The recessive forms for the most part involve mutations in genes encoding components of the dystrophin-associated complex; another form, LGMD2A (OMIM Ref. No. 253600), is caused by mutations in the gene for the muscle-specific protease calpain 3 (CAPN3; 114340). Miyoshi myopathy (MM; 254130) is an adult-onset, recessively inherited distal muscular dystrophy that maps to 2p13. A form of recessive limb-girdle muscular dystrophy, designated LGMD2B (OMIM Ref. No. 253601), maps to the same chromosomal region. This raised the possibility that MM and LGMD2B are allelic

disorders. In fact they were shown to be varying expressions of the same mutant gene; 2 large, inbred kindreds whose members included both MM and LGMD2B patients were described by Weiler et al. (1996) and Illarioshkin et al. (1996, 1997). Affected individuals in both pedigrees shared the same haplotype. Differences in the phenotype appeared to be due to additional modifying factors. Liu et al. (1998) constructed a 3-Mb PAC contig spanning the MM candidate region. This clarified the order of genetic markers across the area, provided 5 new polymorphic markers within it, and narrowed the locus to approximately 2 Mb. They found 5 skeletal muscle ESTs that mapped in this region. Liu et al. (1998) reported that 1 of these ESTs is located in a novel, full-length 6.9-kb muscle cDNA; they designated the corresponding protein dysferlin. Animal model experiments lend further support to the function of DYSF. The SJL mouse strain (Festing, 1979) is susceptible to many induced autoimmune diseases such as experimental autoimmune encephalitis (EAE) and inflammatory muscle disease. Additionally, the skeletal muscle of SJL mice was shown to have an increased regenerative capacity and demonstrates the spontaneous occurrence of what was designated an 'inflammatory my-



opathy,' accompanied by loss of strength. By histopathologic examinations of muscles in SJL mice of different ages, Bittner et al. (1999) found features compatible with a progressive muscular dystrophy, including degenerative and regenerative changes of muscle fibers and a progressive fibrosis. Histologically, the changes were observed in mice as young as 3 weeks of age. Changes affected primarily the proximal muscle groups, whereas the distal muscles remained less affected. The morphologic alterations were associated with signs of slowly progressive muscle weakness, which Bittner et al. (1999) detected as early as 3 weeks after birth when mice were suspended by their tails. The phenotype was found to be inherited as an autosomal recessive trait and was found to map to mouse chromosome 6, in a region syntenic with human 2p13, where the DYSF gene maps. Because of this synteny, Bittner et al. (1999) studied dysferlin in these mice. They found a reduction to approximately 15% of control levels in SJL mice. They found a 171-bp deletion in the *Dysf* gene of SJL mice, predicted to result in removal of 57 amino acids, including most of the fourth C2 domain. The last C2 domain is conserved in other members of the ferlike gene family.

[61997] It is appreciated that the abovementioned animal model for DYSF is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[61998] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[61999] Bittner, R. E.; Anderson, L. V. B.; Burkhardt, E.; Bashir, R.; Vafiadaki, E.; Ivanova, S.; Raffelsberger, T.; Maerk, I.; Hoger, H.; Jung, M.; Karbasiyan, M.; Storch, M.; Lassmann, H.; Moss, J. A.; Davison, K.; Harrison, R.; Bushby, K. M. D.; Reis, A. : Dysferlin deletion in SJL mice (SJL-Dysf) defines a natural model for limb girdle muscular dystrophy 2B. (Letter) Nature Genet. 23: 141–142, 1999. ; and

[62000] Liu, J.; Wu, C.; Bossie, K.; Bejaoui, K.; Hosler, B. A.; Gingrich, J. C.; Ben Hamida, M.; Hentati, F.; Schurr, E.; de Jong, P. J.; Brown, R. H., Jr. : Generation of 3-Mb PAC contig sp.

[62001] Further studies establishing the function and utilities of DYSF are found in John Hopkins OMIM database record ID 603009, and in cited publications numbered 5879, 7234, 7754–7756, 6425, 6427, 7235, 7757–7758, 947 and 7759 listed in the bibliography section hereinbelow, which

are also hereby incorporated by reference. Fibroblast Growth Factor 18 (FGF18, Accession NM\_003862) is another VGAM1869 host target gene. FGF18 BINDING SITE1 and FGF18 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGF18, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF18 BINDING SITE1 and FGF18 BINDING SITE2, designated SEQ ID:9955 and SEQ ID:27383 respectively, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62002] Another function of VGAM1869 is therefore inhibition of Fibroblast Growth Factor 18 (FGF18, Accession NM\_003862), a gene which stimulates hepatic and intestinal proliferation. Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF18. The function of FGF18 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM925.LENG4 (Accession NM\_024298) is another

VGAM1869 host target gene. LENG4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LENG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LENG4 BINDING SITE, designated SEQ ID:23585, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62003] Another function of VGAM1869 is therefore inhibition of LENG4 (Accession NM\_024298), a gene which may be a transmembrane protein. Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LENG4. The function of LENG4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259.V-yes-1 Yamaguchi Sarcoma Viral Related Oncogene Homolog (LYN, Accession NM\_002350) is another VGAM1869 host target gene. LYN BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LYN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LYN BINDING SITE, designated SEQ ID:8153, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62004] Another function of VGAM1869 is therefore inhibition of V–yes–1 Yamaguchi Sarcoma Viral Related Oncogene Homolog (LYN, Accession NM\_002350), a gene which is a Tyrosine kinase with similarity to murine tyrosine kinase p56lck; similar to v–yes protein and the gene products of v–fgr and v–src. Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LYN. The function of LYN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Matrix Metalloproteinase 25 (MMP25, Accession NM\_022468) is another VGAM1869 host target gene. MMP25 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MMP25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MMP25 BINDING SITE, designated SEQ ID:22822, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62005] Another function of VGAM1869 is therefore inhibition of Matrix Metalloproteinase 25 (MMP25, Accession NM\_022468). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP25. Phospholipase A2, Group X (PLA2G10, Accession NM\_003561) is another VGAM1869 host target gene. PLA2G10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLA2G10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2G10 BINDING SITE, designated SEQ ID:9619, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62006] Another function of VGAM1869 is therefore inhibition of Phospholipase A2, Group X (PLA2G10, Accession NM\_003561). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLA2G10. Scratch Homolog

1, Zinc Finger Protein (Drosophila) (SCRT1, Accession NM\_031309) is another VGAM1869 host target gene. SCRT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCRT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCRT1 BINDING SITE, designated SEQ ID:25346, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62007] Another function of VGAM1869 is therefore inhibition of Scratch Homolog 1, Zinc Finger Protein (Drosophila) (SCRT1, Accession NM\_031309), a gene which is involved in the generation and migration of neural crest cells. Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCRT1. The function of SCRT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189. Solute Carrier Family 14 (urea transporter), Member 2 (SLC14A2, Accession NM\_007163) is another VGAM1869 host target gene.

SLC14A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC14A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC14A2 BINDING SITE, designated SEQ ID:14011, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62008] Another function of VGAM1869 is therefore inhibition of Solute Carrier Family 14 (urea transporter), Member 2 (SLC14A2, Accession NM\_007163), a gene which is a renal urea transporter 2. Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC14A2. The function of SLC14A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Survival of Motor Neuron 1, Telomeric (SMN1, Accession NM\_022874) is another VGAM1869 host target gene. SMN1 BINDING SITE1 and SMN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMN1, corresponding to HOST TAR-



GET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMN1 BINDING SITE1 and SMN1 BINDING SITE2, designated SEQ ID:23151 and SEQ ID:5895 respectively, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62009] Another function of VGAM1869 is therefore inhibition of Survival of Motor Neuron 1, Telomeric (SMN1, Accession NM\_022874), a gene which plays an essential role in spliceosomal snrnp assembly in the cytoplasm. Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMN1. The function of SMN1 has been established by previous studies. Lefebvre et al. (1995) described an inverted duplication of a 500-kb element in normal chromosome 5q13 which contains the gene for spinal muscular atrophy, e.g., type I (SMA1; 253300). They further narrowed the critical region to 140 kb within the telomeric portion of this region. This interval was found to contain a 20-kb gene encoding a novel protein of 294 amino acids. A highly homologous gene (SMN2; 601627), referred to as C-BCD541, was present in the duplicated

centromeric element in 95% of controls. The authors suggested that the defect in SMA resides in the telomeric gene, which they found was either lacking or interrupted in 226 of 229 patients. The other 3 patients retaining the gene carried either a point mutation (Y272C; 600354.0004) or short deletions in the consensus splice sites of introns 6 and 7. The gene, designated SMN for survival motor neuron gene, was found to have no homology at either the nucleotide or the amino acid level to sequences in several databases. The SMN gene has 8 exons. SMN interacts with spliceosomal snRNP proteins and is critical for snRNP assembly in the cytoplasm. Pellizzoni et al. (1998) demonstrated that a dominant-negative mutant SMN lacking the first amino-terminal 27 amino acids (SMN $\Delta$ elN27) causes a dramatic reorganization of snRNPs in the nucleus. Furthermore, SMN $\Delta$ elN27 inhibits pre-mRNA splicing in vitro, while wildtype SMN stimulates splicing (using chicken delta-crystallin mRNA as the experimental system). SMN mutants found in SMA patients cannot stimulate splicing. These findings demonstrate that SMN plays a crucial role in the generation of the pre-mRNA splicing machinery and thus in mRNA biogenesis. Animal model experiments lend further support to the

function of SMN1. To understand the functional role of SMN1 in spinal muscular atrophy, Hsieh-Li et al. (2000) produced mouse lines deficient for mouse Smn and transgenic mouse lines that expressed human SMN2. Smn -/- mice died during the peri-implantation stage. In contrast, transgenic mice harboring SMN2 in the Smn -/- background showed pathologic changes in the spinal cord and skeletal muscles similar to those of SMA patients. The severity of the pathologic changes in these mice correlated with the amount of SMN protein that contained the region encoded by exon 7. The results demonstrated that SMN2 can partially compensate for lack of SMN1. The variable phenotypes of Smn -/-SMN2 mice reflected those seen in SMA patients, thus providing a mouse model for that disease.

[62010] It is appreciated that the abovementioned animal model for SMN1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[62011] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[62012] Lefebvre, S.; Burglen, L.; Reboullet, S.; Clermont, O.;

Burlet, P.; Viollet, L.; Benichou, B.; Cruaud, C.; Millasseau, P.; Zeviani, M.; Le Paslier, D.; Frezal, J.; Cohen, D.; Weissenbach, J.; Munnich, A.; Melki, J. : Identification and characterization of a spinal muscular atrophy-determining gene. Cell 80: 155-165, 1995. ; and

[62013] Hsieh-Li, H. M.; Chang, J.-G.; Jong, Y.-J.; Wu, M.-H.; Wang, N. M.; Tsai, C. H.; Li, H. : A mouse model for spinal muscular atrophy. Nature Genet. 24: 66-70, 2000.

[62014] Further studies establishing the function and utilities of SMN1 are found in John Hopkins OMIM database record ID 600354, and in cited publications numbered 8364, 9829-8371, 9237, 9879-9885, 9238, 9886-9888, 9239, 9889-9893, 9240, 9894-9902, 10138, 10160-10172, 673 and 10173 listed in the bibliography section herein-below, which are also hereby incorporated by reference. Centaurin, Beta 5 (CENTB5, Accession XM\_170937) is another VGAM1869 host target gene. CENTB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTB5 BINDING SITE, designated SEQ ID:45724, to the

nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62015] Another function of VGAM1869 is therefore inhibition of Centaurin, Beta 5 (CENTB5, Accession XM\_170937). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTB5. DKFZP434F0318 (Accession NM\_030817) is another VGAM1869 host target gene. DKFZP434F0318 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434F0318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434F0318 BINDING SITE, designated SEQ ID:25142, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62016] Another function of VGAM1869 is therefore inhibition of DKFZP434F0318 (Accession NM\_030817). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434F0318. DKFZp761O0113 (Accession NM\_018409) is another VGAM1869 host target gene. DK-

FZp761O0113 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp761O0113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761O0113 BINDING SITE, designated SEQ ID:20447, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62017] Another function of VGAM1869 is therefore inhibition of DKFZp761O0113 (Accession NM\_018409). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761O0113. FLJ10297 (Accession NM\_018049) is another VGAM1869 host target gene. FLJ10297 BINDING SITE1 and FLJ10297 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10297, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10297 BINDING SITE1 and FLJ10297 BINDING SITE2, designated SEQ ID:19804 and SEQ ID:19806 respectively, to the nucleotide sequence of

VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62018] Another function of VGAM1869 is therefore inhibition of FLJ10297 (Accession NM\_018049). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10297. FLJ12387 (Accession NM\_022822) is another VGAM1869 host target gene. FLJ12387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12387 BINDING SITE, designated SEQ ID:23102, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62019] Another function of VGAM1869 is therefore inhibition of FLJ12387 (Accession NM\_022822). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12387. FLJ12581 (Accession NM\_024865) is another VGAM1869 host target gene. FLJ12581 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ12581, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12581 BINDING SITE, designated SEQ ID:24301, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62020] Another function of VGAM1869 is therefore inhibition of FLJ12581 (Accession NM\_024865). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12581. FLJ14810 (Accession NM\_032843) is another VGAM1869 host target gene. FLJ14810 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14810, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14810 BINDING SITE, designated SEQ ID:26636, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62021] Another function of VGAM1869 is therefore inhibition of FLJ14810 (Accession NM\_032843). Accordingly, utilities of



VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14810. FLJ14834 (Accession NM\_032849) is another VGAM1869 host target gene. FLJ14834 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14834, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14834 BINDING SITE, designated SEQ ID:26643, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62022] Another function of VGAM1869 is therefore inhibition of FLJ14834 (Accession NM\_032849). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14834. FLJ21032 (Accession NM\_024906) is another VGAM1869 host target gene. FLJ21032 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ21032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21032

BINDING SITE, designated SEQ ID:24397, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62023] Another function of VGAM1869 is therefore inhibition of FLJ21032 (Accession NM\_024906). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21032. FLJ22479 (Accession NM\_024900) is another VGAM1869 host target gene. FLJ22479 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22479 BINDING SITE, designated SEQ ID:24385, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62024] Another function of VGAM1869 is therefore inhibition of FLJ22479 (Accession NM\_024900). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22479. HCA4 (Accession XM\_085287) is another VGAM1869 host target gene. HCA4 BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by HCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA4 BINDING SITE, designated SEQ ID:38023, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62025] Another function of VGAM1869 is therefore inhibition of HCA4 (Accession XM\_085287). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCA4. KIAA0089 (Accession XM\_046056) is another VGAM1869 host target gene. KIAA0089 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0089, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0089 BINDING SITE, designated SEQ ID:34665, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62026] Another function of VGAM1869 is therefore inhibition of

KIAA0089 (Accession XM\_046056). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0089. KIAA0557 (Accession XM\_085507) is another VGAM1869 host target gene. KIAA0557 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0557 BINDING SITE, designated SEQ ID:38208, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62027] Another function of VGAM1869 is therefore inhibition of KIAA0557 (Accession XM\_085507). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0557. KIAA1210 (Accession XM\_172801) is another VGAM1869 host target gene. KIAA1210 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1210 BINDING SITE, designated SEQ ID:46087, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62028] Another function of VGAM1869 is therefore inhibition of KIAA1210 (Accession XM\_172801). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1210. KIAA1668 (Accession XM\_039236) is another VGAM1869 host target gene. KIAA1668 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1668 BINDING SITE, designated SEQ ID:33028, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62029] Another function of VGAM1869 is therefore inhibition of KIAA1668 (Accession XM\_039236). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1668. SARM (Accession NM\_015077) is another

VGAM1869 host target gene. SARM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SARM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SARM BINDING SITE, designated SEQ ID:17462, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62030] Another function of VGAM1869 is therefore inhibition of SARM (Accession NM\_015077). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SARM. SNFT (Accession NM\_018664) is another VGAM1869 host target gene. SNFT BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SNFT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNFT BINDING SITE, designated SEQ ID:20743, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62031] Another function of VGAM1869 is therefore inhibition of SNFT (Accession NM\_018664). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNFT. Ubiquitin-like, Containing PHD and RING Finger Domains, 2 (UHRF2, Accession XM\_055929) is another VGAM1869 host target gene. UHRF2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by UHRF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UHRF2 BINDING SITE, designated SEQ ID:36356, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62032] Another function of VGAM1869 is therefore inhibition of Ubiquitin-like, Containing PHD and RING Finger Domains, 2 (UHRF2, Accession XM\_055929). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UHRF2. LOC134121 (Accession XM\_059692) is another VGAM1869 host target gene. LOC134121 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by LOC134121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134121 BINDING SITE, designated SEQ ID:37063, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62033] Another function of VGAM1869 is therefore inhibition of LOC134121 (Accession XM\_059692). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134121. LOC150630 (Accession XM\_097931) is another VGAM1869 host target gene. LOC150630 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150630 BINDING SITE, designated SEQ ID:41241, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62034] Another function of VGAM1869 is therefore inhibition of LOC150630 (Accession XM\_097931). Accordingly, utilities



of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150630. LOC155382 (Accession XM\_098713) is another VGAM1869 host target gene. LOC155382 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC155382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155382 BINDING SITE, designated SEQ ID:41765, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62035] Another function of VGAM1869 is therefore inhibition of LOC155382 (Accession XM\_098713). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155382. LOC203369 (Accession XM\_114689) is another VGAM1869 host target gene. LOC203369 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203369, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC203369 BINDING SITE, designated SEQ ID:43032, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62036] Another function of VGAM1869 is therefore inhibition of LOC203369 (Accession XM\_114689). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203369. LOC203427 (Accession XM\_114699) is another VGAM1869 host target gene. LOC203427 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203427 BINDING SITE, designated SEQ ID:43044, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62037] Another function of VGAM1869 is therefore inhibition of LOC203427 (Accession XM\_114699). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203427. LOC221431 (Accession XM\_166380) is another VGAM1869 host target gene. LOC221431 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221431, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221431 BINDING SITE, designated SEQ ID:44224, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62038] Another function of VGAM1869 is therefore inhibition of LOC221431 (Accession XM\_166380). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221431. LOC254057 (Accession XM\_173085) is another VGAM1869 host target gene. LOC254057 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254057 BINDING SITE, designated SEQ ID:46343, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62039] Another function of VGAM1869 is therefore inhibition of

LOC254057 (Accession XM\_173085). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254057. LOC257486 (Accession XM\_045029) is another VGAM1869 host target gene. LOC257486 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257486 BINDING SITE, designated SEQ ID:34325, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62040] Another function of VGAM1869 is therefore inhibition of LOC257486 (Accession XM\_045029). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257486. LOC91300 (Accession NM\_138774) is another VGAM1869 host target gene. LOC91300 BINDING SITE1 and LOC91300 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC91300, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or

**BINDING SITE III.** Table 2 illustrates the complementarity of the nucleotide sequences of LOC91300 BINDING SITE1 and LOC91300 BINDING SITE2, designated SEQ ID:29006 and SEQ ID:45387 respectively, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62041] Another function of VGAM1869 is therefore inhibition of LOC91300 (Accession NM\_138774). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91300. LOC92697 (Accession XM\_046715) is another VGAM1869 host target gene. LOC92697 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC92697, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92697 BINDING SITE, designated SEQ ID:34804, to the nucleotide sequence of VGAM1869 RNA, herein designated VGAM RNA, also designated SEQ ID:4580.

[62042] Another function of VGAM1869 is therefore inhibition of LOC92697 (Accession XM\_046715). Accordingly, utilities of VGAM1869 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC92697. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1870 (VGAM1870) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62043] VGAM1870 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1870 was detected is described hereinabove with reference to Figs. 1–8.

[62044] VGAM1870 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1870 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62045] VGAM1870 gene encodes a VGAM1870 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1870 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1870 precursor RNA is desig-

nated SEQ ID:1856, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1856 is located at position 190565 relative to the genome of Fowlpox Virus.

- [62046] VGAM1870 precursor RNA folds onto itself, forming VGAM1870 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [62047] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1870 folded precursor RNA into VGAM1870 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1870 RNA is designated SEQ ID:4581, and is provided hereinbelow with reference to the sequence

listing part.

[62048] VGAM1870 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1870 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1870 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62049] VGAM1870 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1870 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1870 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1870 RNA, herein designated VGAM RNA, may



have a different number of host target binding sites in untranslated regions of a VGAM1870 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[62050] The complementary binding of VGAM1870 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1870 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1870 host target RNA into VGAM1870 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62051] It is appreciated that VGAM1870 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1870 host target genes. The mRNA of each one of this plurality of VGAM1870 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1870 RNA, herein designated VGAM

RNA, and which when bound by VGAM1870 RNA causes inhibition of translation of respective one or more VGAM1870 host target proteins.

[62052] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1870 gene, herein designated VGAM GENE, on one or more VGAM1870 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62053] It is yet further appreciated that a function of VGAM1870 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1870 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1870 correlate with, and may be deduced from, the identity of the host target genes which VGAM1870 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62054] Nucleotide sequences of the VGAM1870 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1870 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1870 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1870 are further described hereinbelow with reference to Table 1.

[62055] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1870 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1870 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62056] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1870 gene, herein designated VGAM is

inhibition of expression of VGAM1870 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1870 correlate with, and may be deduced from, the identity of the target genes which VGAM1870 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62057] Zinc Finger Protein 261 (ZNF261, Accession NM\_005096) is a VGAM1870 host target gene. ZNF261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF261 BINDING SITE, designated SEQ ID:11561, to the nucleotide sequence of VGAM1870 RNA, herein designated VGAM RNA, also designated SEQ ID:4581.

[62058] A function of VGAM1870 is therefore inhibition of Zinc Finger Protein 261 (ZNF261, Accession NM\_005096). Accordingly, utilities of VGAM1870 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF261. HTEX4 (Accession XM\_166378) is another VGAM1870 host target gene. HTEX4 BINDING SITE1 through HTEX4 BINDING SITE3 are HOST TARGET

binding sites found in untranslated regions of mRNA encoded by HTEX4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTEX4 BINDING SITE1 through HTEX4 BINDING SITE3, designated SEQ ID:44213, SEQ ID:46718 and SEQ ID:46649 respectively, to the nucleotide sequence of VGAM1870 RNA, herein designated VGAM RNA, also designated SEQ ID:4581.

[62059] Another function of VGAM1870 is therefore inhibition of HTEX4 (Accession XM\_166378). Accordingly, utilities of VGAM1870 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTEX4. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1871 (VGAM1871) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62060] VGAM1871 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1871 was detected is described hereinabove with reference to Figs. 1–8.

[62061] VGAM1871 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1871 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62062] VGAM1871 gene encodes a VGAM1871 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1871 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1871 precursor RNA is designated SEQ ID:1857, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1857 is located at position 195331 relative to the genome of Fowlpox Virus.

[62063] VGAM1871 precursor RNA folds onto itself, forming VGAM1871 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[62064] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1871 folded precursor RNA into VGAM1871 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1871 RNA is designated SEQ ID:4582, and is provided hereinbelow with reference to the sequence listing part.

[62065] VGAM1871 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1871 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1871 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62066] VGAM1871 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1871 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1871 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1871 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1871 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62067] The complementary binding of VGAM1871 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1871 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE



II and BINDING SITE III, inhibits translation of VGAM1871 host target RNA into VGAM1871 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62068] It is appreciated that VGAM1871 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1871 host target genes. The mRNA of each one of this plurality of VGAM1871 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1871 RNA, herein designated VGAM RNA, and which when bound by VGAM1871 RNA causes inhibition of translation of respective one or more VGAM1871 host target proteins.

[62069] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1871 gene, herein designated VGAM GENE, on one or more VGAM1871 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62070] It is yet further appreciated that a function of VGAM1871 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1871 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1871 correlate with, and may be deduced from, the identity of the host target genes which VGAM1871 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62071] Nucleotide sequences of the VGAM1871 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1871 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1871 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1871 are further described hereinbelow with reference to Table 1.

[62072] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1871 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1871 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62073] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1871 gene, herein designated VGAM is inhibition of expression of VGAM1871 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1871 correlate with, and may be deduced from, the identity of the target genes which VGAM1871 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62074] AFAP (Accession NM\_021638) is a VGAM1871 host target gene. AFAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AFAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of AFAP BINDING SITE, designated SEQ ID:22288, to the nucleotide sequence of VGAM1871 RNA, herein designated VGAM RNA, also designated SEQ ID:4582.

[62075] A function of VGAM1871 is therefore inhibition of AFAP (Accession NM\_021638). Accordingly, utilities of VGAM1871 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AFAP. ARP3BETA (Accession NM\_020445) is another VGAM1871 host target gene. ARP3BETA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARP3BETA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARP3BETA BINDING SITE, designated SEQ ID:21686, to the nucleotide sequence of VGAM1871 RNA, herein designated VGAM RNA, also designated SEQ ID:4582.

[62076] Another function of VGAM1871 is therefore inhibition of ARP3BETA (Accession NM\_020445). Accordingly, utilities of VGAM1871 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARP3BETA. MSTP032 (Accession NM\_025226) is another VGAM1871 host target gene. MSTP032 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSTP032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSTP032 BINDING SITE, designated SEQ ID:24905, to the nucleotide sequence of VGAM1871 RNA, herein designated VGAM RNA, also designated SEQ ID:4582.

[62077] Another function of VGAM1871 is therefore inhibition of MSTP032 (Accession NM\_025226). Accordingly, utilities of VGAM1871 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSTP032. Pleckstrin Homology Domain Containing, Family A (phosphoinositide binding specific) Member 3 (PLEKHA3, Accession NM\_019091) is another VGAM1871 host target gene. PLEKHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLEKHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLEKHA3 BINDING SITE, designated SEQ ID:21168, to the nucleotide sequence of VGAM1871 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4582.

[62078] Another function of VGAM1871 is therefore inhibition of Pleckstrin Homology Domain Containing, Family A (phosphoinositide binding specific) Member 3 (PLEKHA3, Accession NM\_019091). Accordingly, utilities of VGAM1871 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLEKHA3. PRO2133 (Accession NM\_018619) is another VGAM1871 host target gene. PRO2133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2133 BINDING SITE, designated SEQ ID:20690, to the nucleotide sequence of VGAM1871 RNA, herein designated VGAM RNA, also designated SEQ ID:4582.

[62079] Another function of VGAM1871 is therefore inhibition of PRO2133 (Accession NM\_018619). Accordingly, utilities of VGAM1871 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2133. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1872 (VGAM1872) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62080] VGAM1872 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1872 was detected is described hereinabove with reference to Figs. 1–8.

[62081] VGAM1872 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1872 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62082] VGAM1872 gene encodes a VGAM1872 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1872 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1872 precursor RNA is designated SEQ ID:1858, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1858 is located at position 190660 relative to the

genome of Fowlpox Virus.

[62083] VGAM1872 precursor RNA folds onto itself, forming VGAM1872 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62084] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1872 folded precursor RNA into VGAM1872 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1872 RNA is designated SEQ ID:4583, and is provided hereinbelow with reference to the sequence listing part.

[62085] VGAM1872 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1872 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1872 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[62086] VGAM1872 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1872 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1872 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1872 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1872 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[62087] The complementary binding of VGAM1872 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1872 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1872 host target RNA into VGAM1872 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62088] It is appreciated that VGAM1872 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1872 host target genes. The mRNA of each one of this plurality of VGAM1872 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1872 RNA, herein designated VGAM RNA, and which when bound by VGAM1872 RNA causes inhibition of translation of respective one or more VGAM1872 host target proteins.

[62089] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1872 gene, herein designated VGAM GENE, on one or more VGAM1872 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62090] It is yet further appreciated that a function of VGAM1872 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1872 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1872 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1872 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62091] Nucleotide sequences of the VGAM1872 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1872 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1872 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1872 are further described hereinbelow with reference to Table 1.

[62092] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1872 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1872 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62093] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1872 gene, herein designated VGAM is inhibition of expression of VGAM1872 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1872 correlate with, and may be deduced

from, the identity of the target genes which VGAM1872 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62094] Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3A (glycogen and sarcoplasmic reticulum binding subunit, skeletal muscle) (PPP1R3A, Accession NM\_002711) is a VGAM1872 host target gene. PPP1R3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R3A BINDING SITE, designated SEQ ID:8566, to the nucleotide sequence of VGAM1872 RNA, herein designated VGAM RNA, also designated SEQ ID:4583.

[62095] A function of VGAM1872 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3A (glycogen and sarcoplasmic reticulum binding subunit, skeletal muscle) (PPP1R3A, Accession NM\_002711), a gene which regulates phosphatase activity towards glycogen synthase, active in skeletal muscle. Accordingly, utilities of VGAM1872 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PPP1R3A. The function of PPP1R3A has been established by previous studies. The glycogen-associated form of protein phosphatase-1 (PP1) derived from skeletal muscle is a heterodimer composed of a 37-kD catalytic subunit (OMIM Ref. No. 176875) and a 124-kD targeting and regulatory subunit, referred to as PP1G by Hansen et al. (1995). PP1G binds to muscle glycogen with high affinity, thereby enhancing dephosphorylation of glycogen-bound substrates for PP1 such as glycogen synthase (e.g., 138570) and glycogen phosphorylase kinase (e.g., 306000). Phosphorylation at ser46 of the PP1G subunit in response to insulin increases PP1 activity, while phosphorylation at ser65 in response to adrenaline causes dissociation of the catalytic subunit from the G subunit and inhibits glycogen synthesis. Because of these functions, PP1G was postulated to be involved in noninsulin-dependent diabetes mellitus (NIDDM; 125853) and obesity. Savage et al. (2002) described an example of digenic inheritance of severe insulin resistance. In a family they referred to as 'a Euroid pedigree' they found 5 members with severe insulin resistance and heterozygosity for frameshift/premature stop mutations in each of 2 unlinked genes, PPARC (601487.0011) and PPP1R3A (600917.0003).

PPARG is highly expressed in adipocytes, and PPP1R3A, the muscle-specific regulatory subunit of protein phosphatase 1, is centrally involved in the regulation of carbohydrate and lipid metabolism, respectively. That mutant molecules primarily involved in either carbohydrate or lipid metabolism can combine to produce a phenotype of extreme insulin resistance provides a model of interaction among genes that may underlie common human metabolic disorders such as type 2 diabetes (NIDDM). In the Euroid family reported by Savage et al. (2002), the grandfather was heterozygous for the PPARG mutation, the grandmother was heterozygous for the PPP1R3A mutation. Three of their children and 2 of their grandchildren carried both mutations in heterozygous state, and all 5, but only these 5, had severe insulin resistance manifest by acanthosis nigricans, a dermatologic marker of extreme insulin resistance, and markedly elevated fasting plasma insulin levels.

[62096] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[62097] Savage, D. B.; Agostini, M.; Barroso, I.; Gurnell, M.; Luan, J.; Meirhaeghe, A.; Harding, A.-H.; Ihrke, G.; Rajanayagam,

O.; Soos, M. A.; George, S.; Berger, D.; and 9 others : Di-genic inheritance of severe insulin resistance in a human pedigree. Nature Genet. 31: 379–384, 2002. ; and

[62098] Tang, P. M.; Bondor, J. A.; Swiderek, K. M.; DePaoli-Roach, A. A. : Molecular cloning and expression of the regulatory (RG1) subunit of the glycogen-associated protein phosphatase. J. B.

[62099] Further studies establishing the function and utilities of PPP1R3A are found in John Hopkins OMIM database record ID 600917, and in cited publications numbered 9926, 9953–995 and 9954 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protease, Serine, 16 (thymus) (PRSS16, Accession NM\_005865) is another VGAM1872 host target gene. PRSS16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRSS16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRSS16 BINDING SITE, designated SEQ ID:12483, to the nucleotide sequence of VGAM1872 RNA, herein designated VGAM RNA, also designated SEQ ID:4583.



[62100] Another function of VGAM1872 is therefore inhibition of Protease, Serine, 16 (thymus) (PRSS16, Accession NM\_005865). Accordingly, utilities of VGAM1872 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRSS16. FLJ13576 (Accession NM\_022484) is another VGAM1872 host target gene. FLJ13576 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13576 BINDING SITE, designated SEQ ID:22861, to the nucleotide sequence of VGAM1872 RNA, herein designated VGAM RNA, also designated SEQ ID:4583.

[62101] Another function of VGAM1872 is therefore inhibition of FLJ13576 (Accession NM\_022484). Accordingly, utilities of VGAM1872 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13576. KIAA0372 (Accession NM\_014639) is another VGAM1872 host target gene. KIAA0372 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0372, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0372 BINDING SITE, designated SEQ ID:16038, to the nucleotide sequence of VGAM1872 RNA, herein designated VGAM RNA, also designated SEQ ID:4583.

[62102] Another function of VGAM1872 is therefore inhibition of KIAA0372 (Accession NM\_014639). Accordingly, utilities of VGAM1872 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0372. KIAA1361 (Accession XM\_030845) is another VGAM1872 host target gene. KIAA1361 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1361 BINDING SITE, designated SEQ ID:31173, to the nucleotide sequence of VGAM1872 RNA, herein designated VGAM RNA, also designated SEQ ID:4583.

[62103] Another function of VGAM1872 is therefore inhibition of KIAA1361 (Accession XM\_030845). Accordingly, utilities of VGAM1872 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1361. LOC222060 (Accession XM\_168427) is another VGAM1872 host target gene. LOC222060 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222060 BINDING SITE, designated SEQ ID:45161, to the nucleotide sequence of VGAM1872 RNA, herein designated VGAM RNA, also designated SEQ ID:4583.

[62104] Another function of VGAM1872 is therefore inhibition of LOC222060 (Accession XM\_168427). Accordingly, utilities of VGAM1872 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222060. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1873 (VGAM1873) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62105] VGAM1873 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1873 was detected is described hereinabove with reference to Figs. 1–8.

[62106] VGAM1873 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1873 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62107] VGAM1873 gene encodes a VGAM1873 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1873 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1873 precursor RNA is designated SEQ ID:1859, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1859 is located at position 188015 relative to the genome of Fowlpox Virus.

[62108] VGAM1873 precursor RNA folds onto itself, forming VGAM1873 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62109] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1873 folded precursor RNA into VGAM1873 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 64%) nucleotide sequence of VGAM1873 RNA is designated SEQ ID:4584, and is provided hereinbelow with reference to the sequence listing part.

[62110] VGAM1873 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1873 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1873 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62111] VGAM1873 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1873 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1873 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1873 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1873 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62112] The complementary binding of VGAM1873 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1873 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1873 host target RNA into VGAM1873 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62113] It is appreciated that VGAM1873 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1873 host target genes. The mRNA of each one of this plurality of VGAM1873 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1873 RNA, herein designated VGAM RNA, and which when bound by VGAM1873 RNA causes inhibition of translation of respective one or more VGAM1873 host target proteins.

[62114] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1873 gene, herein designated VGAM GENE, on one or more VGAM1873 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62115] It is yet further appreciated that a function of VGAM1873 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1873 correlate with, and may be deduced from, the identity of the host target genes which VGAM1873 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62116] Nucleotide sequences of the VGAM1873 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the



`diced` VGAM1873 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1873 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1873 are further described hereinbelow with reference to Table 1.

[62117] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1873 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1873 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62118] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1873 gene, herein designated VGAM is inhibition of expression of VGAM1873 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1873 correlate with, and may be deduced from, the identity of the target genes which VGAM1873 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62119] Engulfment and Cell Motility 1 (ced-12 homolog, *C. elegans*) (ELMO1, Accession NM\_130442) is a VGAM1873 host target gene. ELMO1 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by ELMO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELMO1 BINDING SITE, designated SEQ ID:28204, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62120] A function of VGAM1873 is therefore inhibition of Engulfment and Cell Motility 1 (ced-12 homolog, *C. elegans*) (ELMO1, Accession NM\_130442). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELMO1. Ectodermal-neural Cortex (with BTB-like domain) (ENC1, Accession NM\_003633) is another VGAM1873 host target gene. ENC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENC1 BINDING SITE, designated SEQ ID:9697, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62121] Another function of VGAM1873 is therefore inhibition of Ectodermal–neural Cortex (with BTB–like domain) (ENC1, Accession NM\_003633), a gene which is an actin–binding protein involved in the regulation of neuronal process formation and in differentiation of neural crest cells. Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENC1. The function of ENC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM233. Heparanase (HPSE, Accession NM\_006665) is another VGAM1873 host target gene. HPSE BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HPSE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPSE BINDING SITE, designated SEQ ID:13475, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62122] Another function of VGAM1873 is therefore inhibition of Heparanase (HPSE, Accession NM\_006665), a gene which is an endoglycosidase that cleaves heparan sulfate. Ac–

cordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPSE. The function of HPSE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM374. RAB3B, Member RAS Oncogene Family (RAB3B, Accession NM\_002867) is another VGAM1873 host target gene. RAB3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB3B BINDING SITE, designated SEQ ID:8771, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62123] Another function of VGAM1873 is therefore inhibition of RAB3B, Member RAS Oncogene Family (RAB3B, Accession NM\_002867). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB3B. Solute Carrier Family 16 (monocarboxylic acid transporters), Member 1 (SLC16A1, Accession NM\_003051) is another VGAM1873

host target gene. SLC16A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC16A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC16A1 BINDING SITE, designated SEQ ID:9012, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62124] Another function of VGAM1873 is therefore inhibition of Solute Carrier Family 16 (monocarboxylic acid transporters), Member 1 (SLC16A1, Accession NM\_003051), a gene which is a Proton-monocarboxylate cotransporter that transports lactate and pyruvate. Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC16A1. The function of SLC16A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM140. Zinc Finger Protein 268 (ZNF268, Accession XM\_031851) is another VGAM1873 host target gene. ZNF268 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by ZNF268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF268 BINDING SITE, designated SEQ ID:31500, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62125] Another function of VGAM1873 is therefore inhibition of Zinc Finger Protein 268 (ZNF268, Accession XM\_031851). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF268. Ras Homolog Gene Family, Member E (ARHE, Accession NM\_005168) is another VGAM1873 host target gene. ARHE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHE BINDING SITE, designated SEQ ID:11668, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62126] Another function of VGAM1873 is therefore inhibition of

Ras Homolog Gene Family, Member E (ARHE, Accession NM\_005168). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHE. FLJ12934 (Accession NM\_022899) is another VGAM1873 host target gene. FLJ12934 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12934 BINDING SITE, designated SEQ ID:23175, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62127] Another function of VGAM1873 is therefore inhibition of FLJ12934 (Accession NM\_022899). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12934. HCA4 (Accession XM\_085287) is another VGAM1873 host target gene. HCA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA4 BINDING SITE, designated SEQ ID:38030, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62128] Another function of VGAM1873 is therefore inhibition of HCA4 (Accession XM\_085287). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCA4. KIAA0427 (Accession NM\_014772) is another VGAM1873 host target gene. KIAA0427 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0427 BINDING SITE, designated SEQ ID:16571, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62129] Another function of VGAM1873 is therefore inhibition of KIAA0427 (Accession NM\_014772). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



KIAA0427. LOC116228 (Accession XM\_057659) is another VGAM1873 host target gene. LOC116228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116228 BINDING SITE, designated SEQ ID:36533, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62130] Another function of VGAM1873 is therefore inhibition of LOC116228 (Accession XM\_057659). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116228. LOC221540 (Accession XM\_168133) is another VGAM1873 host target gene. LOC221540 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221540 BINDING SITE, designated SEQ ID:45044, to the nucleotide sequence of VGAM1873 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4584.

[62131] Another function of VGAM1873 is therefore inhibition of LOC221540 (Accession XM\_168133). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221540. LOC257545 (Accession XM\_175217) is another VGAM1873 host target gene. LOC257545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257545 BINDING SITE, designated SEQ ID:46692, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62132] Another function of VGAM1873 is therefore inhibition of LOC257545 (Accession XM\_175217). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257545. LOC257598 (Accession XM\_175295) is another VGAM1873 host target gene. LOC257598 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257598, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257598 BINDING SITE, designated SEQ ID:46749, to the nucleotide sequence of VGAM1873 RNA, herein designated VGAM RNA, also designated SEQ ID:4584.

[62133] Another function of VGAM1873 is therefore inhibition of LOC257598 (Accession XM\_175295). Accordingly, utilities of VGAM1873 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257598. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1874 (VGAM1874) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62134] VGAM1874 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1874 was detected is described hereinabove with reference to Figs. 1-8.

[62135] VGAM1874 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1874 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62136] VGAM1874 gene encodes a VGAM1874 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1874 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1874 precursor RNA is designated SEQ ID:1860, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1860 is located at position 196857 relative to the genome of Fowlpox Virus.

[62137] VGAM1874 precursor RNA folds onto itself, forming VGAM1874 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62138] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1874 folded precursor RNA into VGAM1874 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1874 RNA is designated SEQ ID:4585, and is provided hereinbelow with reference to the sequence listing part.

[62139] VGAM1874 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1874 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1874 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62140] VGAM1874 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1874 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1874 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1874 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1874 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62141] The complementary binding of VGAM1874 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1874 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1874 host target RNA into VGAM1874 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62142] It is appreciated that VGAM1874 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1874 host target genes. The mRNA of each one of this plurality of VGAM1874 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1874 RNA, herein designated VGAM RNA, and which when bound by VGAM1874 RNA causes inhibition of translation of respective one or more VGAM1874 host target proteins.

[62143] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1874 gene, herein designated VGAM GENE, on one or more VGAM1874 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62144] It is yet further appreciated that a function of VGAM1874 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1874 correlate with, and may be deduced from, the identity of the host target genes which VGAM1874 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62145] Nucleotide sequences of the VGAM1874 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1874 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1874 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1874 are further described hereinbelow with reference to Table 1.



[62146] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1874 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1874 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62147] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1874 gene, herein designated VGAM is inhibition of expression of VGAM1874 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1874 correlate with, and may be deduced from, the identity of the target genes which VGAM1874 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62148] Carcinoembryonic Antigen-related Cell Adhesion Molecule 6 (non-specific cross reacting antigen) (CEACAM6, Accession NM\_002483) is a VGAM1874 host target gene. CEACAM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CEACAM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of CEACAM6 BINDING SITE, designated SEQ ID:8307, to the nucleotide sequence of VGAM1874 RNA, herein designated VGAM RNA, also designated SEQ ID:4585.

[62149] A function of VGAM1874 is therefore inhibition of Carcinoembryonic Antigen-related Cell Adhesion Molecule 6 (non-specific cross reacting antigen) (CEACAM6, Accession NM\_002483), a gene which Non-specific cross reacting antigen (. Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEACAM6. The function of CEACAM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM286. Matrix Metalloproteinase 19 (MMP19, Accession NM\_022790) is another VGAM1874 host target gene. MMP19 BINDING SITE1 and MMP19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MMP19, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP19 BINDING SITE1 and MMP19 BINDING SITE2, designated SEQ

ID:23072 and SEQ ID:23081 respectively, to the nucleotide sequence of VGAM1874 RNA, herein designated VGAM RNA, also designated SEQ ID:4585.

[62150] Another function of VGAM1874 is therefore inhibition of Matrix Metalloproteinase 19 (MMP19, Accession NM\_022790). Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP19. DREV1 (Accession NM\_016025) is another VGAM1874 host target gene. DREV1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DREV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DREV1 BINDING SITE, designated SEQ ID:18106, to the nucleotide sequence of VGAM1874 RNA, herein designated VGAM RNA, also designated SEQ ID:4585.

[62151] Another function of VGAM1874 is therefore inhibition of DREV1 (Accession NM\_016025). Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DREV1. Potassium Voltage-gated Channel, Isk-related Family,

Member 4 (KCNE4, Accession NM\_080671) is another VGAM1874 host target gene. KCNE4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KCNE4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNE4 BINDING SITE, designated SEQ ID:27967, to the nucleotide sequence of VGAM1874 RNA, herein designated VGAM RNA, also designated SEQ ID:4585.

[62152] Another function of VGAM1874 is therefore inhibition of Potassium Voltage-gated Channel, Isk-related Family, Member 4 (KCNE4, Accession NM\_080671). Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNE4. Phospholipid Scramblase 4 (PLSCR4, Accession NM\_020353) is another VGAM1874 host target gene. PLSCR4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PLSCR4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLSCR4 BINDING SITE, designated SEQ

ID:21619, to the nucleotide sequence of VGAM1874 RNA, herein designated VGAM RNA, also designated SEQ ID:4585.

[62153] Another function of VGAM1874 is therefore inhibition of Phospholipid Scramblase 4 (PLSCR4, Accession NM\_020353). Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLSCR4. LOC163033 (Accession XM\_091949) is another VGAM1874 host target gene. LOC163033 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163033, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163033 BINDING SITE, designated SEQ ID:40072, to the nucleotide sequence of VGAM1874 RNA, herein designated VGAM RNA, also designated SEQ ID:4585.

[62154] Another function of VGAM1874 is therefore inhibition of LOC163033 (Accession XM\_091949). Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163033. LOC219920 (Accession XM\_167787) is an-

other VGAM1874 host target gene. LOC219920 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219920 BINDING SITE, designated SEQ ID:44801, to the nucleotide sequence of VGAM1874 RNA, herein designated VGAM RNA, also designated SEQ ID:4585.

[62155] Another function of VGAM1874 is therefore inhibition of LOC219920 (Accession XM\_167787). Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219920. LOC253598 (Accession XM\_175049) is another VGAM1874 host target gene. LOC253598 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253598 BINDING SITE, designated SEQ ID:46609, to the nucleotide sequence of VGAM1874 RNA, herein designated VGAM RNA, also designated SEQ ID:4585.

[62156] Another function of VGAM1874 is therefore inhibition of LOC253598 (Accession XM\_175049). Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253598. LOC254173 (Accession XM\_173022) is another VGAM1874 host target gene. LOC254173 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254173 BINDING SITE, designated SEQ ID:46285, to the nucleotide sequence of VGAM1874 RNA, herein designated VGAM RNA, also designated SEQ ID:4585.

[62157] Another function of VGAM1874 is therefore inhibition of LOC254173 (Accession XM\_173022). Accordingly, utilities of VGAM1874 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254173. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1875 (VGAM1875) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[62158] VGAM1875 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1875 was detected is described hereinabove with reference to Figs. 1-8.

[62159] VGAM1875 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1875 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62160] VGAM1875 gene encodes a VGAM1875 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1875 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1875 precursor RNA is designated SEQ ID:1861, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1861 is located at position 187831 relative to the genome of Fowlpox Virus.

[62161] VGAM1875 precursor RNA folds onto itself, forming VGAM1875 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62162] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1875 folded precursor RNA into VGAM1875 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 62%) nucleotide sequence of VGAM1875 RNA is designated SEQ ID:4586, and is provided hereinbelow with reference to the sequence listing part.

[62163] VGAM1875 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1875 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1875 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62164] VGAM1875 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1875 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1875 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1875 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1875 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62165] The complementary binding of VGAM1875 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1875 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1875 host target RNA into VGAM1875 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62166] It is appreciated that VGAM1875 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1875 host target genes. The mRNA of each one of this plurality of VGAM1875 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1875 RNA, herein designated VGAM RNA, and which when bound by VGAM1875 RNA causes inhibition of translation of respective one or more VGAM1875 host target proteins.

[62167] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1875 gene, herein designated VGAM GENE, on one or more VGAM1875 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62168] It is yet further appreciated that a function of VGAM1875 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1875 correlate with, and may be deduced from, the identity of the host target genes which VGAM1875 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[62169] Nucleotide sequences of the VGAM1875 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1875 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1875 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1875 are further described hereinbelow with reference to Table 1.

[62170] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1875 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1875 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62171] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1875 gene, herein designated VGAM is inhibition of expression of VGAM1875 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1875 correlate with, and may be deduced from, the identity of the target genes which VGAM1875 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62172] Cadherin 13, H-cadherin (heart) (CDH13, Accession NM\_001257) is a VGAM1875 host target gene. CDH13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDH13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH13 BINDING SITE, designated SEQ ID:6925, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62173] A function of VGAM1875 is therefore inhibition of Cadherin 13, H-cadherin (heart) (CDH13, Accession NM\_001257). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH13. Coagulation Factor XIII, A1 Polypeptide (F13A1, Accession XM\_165833) is another VGAM1875 host target gene. F13A1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by F13A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F13A1 BINDING SITE, designated SEQ ID:43774, to the nucleotide se-

quence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62174] Another function of VGAM1875 is therefore inhibition of Coagulation Factor XIII, A1 Polypeptide (F13A1, Accession XM\_165833). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F13A1. Heparanase (HPSE, Accession NM\_006665) is another VGAM1875 host target gene. HPSE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPSE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPSE BINDING SITE, designated SEQ ID:13482, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62175] Another function of VGAM1875 is therefore inhibition of Heparanase (HPSE, Accession NM\_006665), a gene which is an endoglycosidase that cleaves heparan sulfate. Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPSE. The function of HPSE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM374. Palmitoyl-protein Thioesterase 2 (PPT2, Accession NM\_138717) is another VGAM1875 host target gene. PPT2 BINDING SITE1 and PPT2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PPT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPT2 BINDING SITE1 and PPT2 BINDING SITE2, designated SEQ ID:28965 and SEQ ID:11634 respectively, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62176] Another function of VGAM1875 is therefore inhibition of Palmitoyl-protein Thioesterase 2 (PPT2, Accession NM\_138717), a gene which is a palmitoyl-protein



thioesterase 2 which possesses a different substrate specificity than PPT1. Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPT2. The function of PPT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120.KIAA0836 (Accession XM\_035390) is another VGAM1875 host target gene. KIAA0836 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0836 BINDING SITE, designated SEQ ID:32247, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62177] Another function of VGAM1875 is therefore inhibition of KIAA0836 (Accession XM\_035390). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0836. KIAA0953 (Accession XM\_039733) is another VGAM1875 host target gene. KIAA0953 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0953, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0953 BINDING SITE, designated SEQ ID:33168, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62178] Another function of VGAM1875 is therefore inhibition of KIAA0953 (Accession XM\_039733). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0953. PRO2958 (Accession NM\_018546) is another VGAM1875 host target gene. PRO2958 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO2958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2958 BINDING SITE, designated SEQ ID:20624, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62179] Another function of VGAM1875 is therefore inhibition of

PRO2958 (Accession NM\_018546). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2958. Serologically Defined Colon Cancer Antigen 1 (SDCCAG1, Accession NM\_004713) is another VGAM1875 host target gene. SDCCAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDCCAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDCCAG1 BINDING SITE, designated SEQ ID:11070, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62180] Another function of VGAM1875 is therefore inhibition of Serologically Defined Colon Cancer Antigen 1 (SDCCAG1, Accession NM\_004713). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDCCAG1. Syntrophin, Gamma 1 (SNTG1, Accession NM\_018967) is another VGAM1875 host target gene. SNTG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

SNTG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNTG1 BINDING SITE, designated SEQ ID:21037, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62181] Another function of VGAM1875 is therefore inhibition of Syntrophin, Gamma 1 (SNTG1, Accession NM\_018967). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNTG1. LOC120856 (Accession XM\_058509) is another VGAM1875 host target gene. LOC120856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120856 BINDING SITE, designated SEQ ID:36642, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62182] Another function of VGAM1875 is therefore inhibition of

LOC120856 (Accession XM\_058509). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120856. LOC131744 (Accession XM\_067529) is another VGAM1875 host target gene. LOC131744 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC131744, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131744 BINDING SITE, designated SEQ ID:37358, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62183] Another function of VGAM1875 is therefore inhibition of LOC131744 (Accession XM\_067529). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131744. LOC147172 (Accession XM\_085729) is another VGAM1875 host target gene. LOC147172 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC147172 BINDING SITE, designated SEQ ID:38313, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62184] Another function of VGAM1875 is therefore inhibition of LOC147172 (Accession XM\_085729). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147172. LOC152195 (Accession XM\_098172) is another VGAM1875 host target gene. LOC152195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152195 BINDING SITE, designated SEQ ID:41435, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62185] Another function of VGAM1875 is therefore inhibition of LOC152195 (Accession XM\_098172). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152195. LOC153454 (Accession XM\_087672) is an-

other VGAM1875 host target gene. LOC153454 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153454, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153454 BINDING SITE, designated SEQ ID:39375, to the nucleotide sequence of VGAM1875 RNA, herein designated VGAM RNA, also designated SEQ ID:4586.

[62186] Another function of VGAM1875 is therefore inhibition of LOC153454 (Accession XM\_087672). Accordingly, utilities of VGAM1875 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153454. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1876 (VGAM1876) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62187] VGAM1876 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1876 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[62188] VGAM1876 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus.

VGAM1876 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62189] VGAM1876 gene encodes a VGAM1876 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1876 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1876 precursor RNA is designated SEQ ID:1862, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1862 is located at position 194761 relative to the genome of Fowlpox Virus.

[62190] VGAM1876 precursor RNA folds onto itself, forming VGAM1876 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA



gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62191] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1876 folded precursor RNA into VGAM1876 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1876 RNA is designated SEQ ID:4587, and is provided hereinbelow with reference to the sequence listing part.

[62192] VGAM1876 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1876 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1876 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62193] VGAM1876 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1876 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1876 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1876 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1876 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62194] The complementary binding of VGAM1876 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1876 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1876 host target RNA into VGAM1876 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62195] It is appreciated that VGAM1876 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1876 host target genes. The mRNA of each one of this plurality of VGAM1876 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1876 RNA, herein designated VGAM RNA, and which when bound by VGAM1876 RNA causes inhibition of translation of respective one or more VGAM1876 host target proteins.

[62196] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1876 gene, herein designated VGAM GENE, on one or more VGAM1876 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62197] It is yet further appreciated that a function of VGAM1876 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1876 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1876 correlate with, and may be deduced from, the identity of the host target genes which VGAM1876 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62198] Nucleotide sequences of the VGAM1876 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1876 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1876 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1876 are further described hereinbelow with reference to Table 1.

[62199] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1876 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1876 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62200] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1876 gene, herein designated VGAM is inhibition of expression of VGAM1876 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1876 correlate with, and may be deduced from, the identity of the target genes which VGAM1876 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62201] Complement Component 7 (C7, Accession NM\_000587) is a VGAM1876 host target gene. C7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C7 BINDING SITE, designated SEQ ID:6188, to the nucleotide sequence of VGAM1876 RNA, herein designated VGAM RNA, also designated SEQ ID:4587.

[62202] A function of VGAM1876 is therefore inhibition of Complement Component 7 (C7, Accession NM\_000587). Accordingly, utilities of VGAM1876 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C7. Calumenin (CALU, Accession NM\_001219) is another VGAM1876 host target gene. CALU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALU BINDING SITE, designated SEQ ID:6884, to the nucleotide sequence of VGAM1876 RNA, herein designated VGAM RNA, also designated SEQ ID:4587.

[62203] Another function of VGAM1876 is therefore inhibition of Calumenin (CALU, Accession NM\_001219), a gene which binds 7 calcium ions with a low affinity with unidentified function. Accordingly, utilities of VGAM1876 include diag-

nosis, prevention and treatment of diseases and clinical conditions associated with CALU. The function of CALU and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM253. Heparanase (HPSE, Accession NM\_006665) is another VGAM1876 host target gene. HPSE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPSE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPSE BINDING SITE, designated SEQ ID:13478, to the nucleotide sequence of VGAM1876 RNA, herein designated VGAM RNA, also designated SEQ ID:4587.

[62204] Another function of VGAM1876 is therefore inhibition of Heparanase (HPSE, Accession NM\_006665), a gene which is an endoglycosidase that cleaves heparan sulfate. Accordingly, utilities of VGAM1876 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPSE. The function of HPSE and its association with various diseases and clinical conditions, has been established by previous studies, as described here-

inabove with reference to VGAM374. Prostaglandin F Receptor (FP) (PTGFR, Accession NM\_000959) is another VGAM1876 host target gene. PTGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGFR BINDING SITE, designated SEQ ID:6662, to the nucleotide sequence of VGAM1876 RNA, herein designated VGAM RNA, also designated SEQ ID:4587.

[62205] Another function of VGAM1876 is therefore inhibition of Prostaglandin F Receptor (FP) (PTGFR, Accession NM\_000959), a gene which mediates intracellular calcium flux, strongly similar to murine Ptgfr. Accordingly, utilities of VGAM1876 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGFR. The function of PTGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1781. RAB18, Member RAS Oncogene Family (RAB18, Accession NM\_021252) is another VGAM1876 host target gene. RAB18 BINDING SITE is HOST



TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB18 BINDING SITE, designated SEQ ID:22220, to the nucleotide sequence of VGAM1876 RNA, herein designated VGAM RNA, also designated SEQ ID:4587.

[62206] Another function of VGAM1876 is therefore inhibition of RAB18, Member RAS Oncogene Family (RAB18, Accession NM\_021252), a gene which plays a role in apical endocytosis/recycling. Accordingly, utilities of VGAM1876 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB18. The function of RAB18 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120.C1q and Tumor Necrosis Factor Related Protein 7 (C1QTNF7, Accession NM\_031911) is another VGAM1876 host target gene. C1QTNF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1QTNF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QTNF7 BINDING SITE, designated SEQ ID:25664, to the nucleotide sequence of VGAM1876 RNA, herein designated VGAM RNA, also designated SEQ ID:4587.

[62207] Another function of VGAM1876 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 7 (C1QTNF7, Accession NM\_031911). Accordingly, utilities of VGAM1876 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF7. FLJ13340 (Accession NM\_057175) is another VGAM1876 host target gene. FLJ13340 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13340 BINDING SITE, designated SEQ ID:27708, to the nucleotide sequence of VGAM1876 RNA, herein designated VGAM RNA, also designated SEQ ID:4587.

[62208] Another function of VGAM1876 is therefore inhibition of FLJ13340 (Accession NM\_057175). Accordingly, utilities of VGAM1876 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ13340. FLJ14621 (Accession NM\_032811) is another VGAM1876 host target gene. FLJ14621 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14621, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14621 BINDING SITE, designated SEQ ID:26579, to the nucleotide sequence of VGAM1876 RNA, herein designated VGAM RNA, also designated SEQ ID:4587.

[62209] Another function of VGAM1876 is therefore inhibition of FLJ14621 (Accession NM\_032811). Accordingly, utilities of VGAM1876 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14621. TBDN100 (Accession NM\_025085) is another VGAM1876 host target gene. TBDN100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBDN100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBDN100 BINDING SITE, designated SEQ ID:24699, to the nucleotide

sequence of VGAM1876 RNA, herein designated VGAM RNA, also designated SEQ ID:4587.

[62210] Another function of VGAM1876 is therefore inhibition of TBDN100 (Accession NM\_025085). Accordingly, utilities of VGAM1876 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBDN100. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1877 (VGAM1877) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62211] VGAM1877 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1877 was detected is described hereinabove with reference to Figs. 1–8.

[62212] VGAM1877 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1877 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62213] VGAM1877 gene encodes a VGAM1877 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1877 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1877 precursor RNA is designated SEQ ID:1863, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1863 is located at position 184855 relative to the genome of Fowlpox Virus.

- [62214] VGAM1877 precursor RNA folds onto itself, forming VGAM1877 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [62215] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1877 folded precursor RNA into VGAM1877 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1877 RNA is designated SEQ ID:4588, and is provided hereinbelow with reference to the sequence listing part.

[62216] VGAM1877 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1877 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1877 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62217] VGAM1877 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1877 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1877 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1877 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1877 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62218] The complementary binding of VGAM1877 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1877 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1877 host target RNA into VGAM1877 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62219] It is appreciated that VGAM1877 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1877 host target genes. The mRNA of each one of this plurality of VGAM1877 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1877 RNA, herein designated VGAM RNA, and which when bound by VGAM1877 RNA causes inhibition of translation of respective one or more VGAM1877 host target proteins.

[62220] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1877 gene, herein designated VGAM GENE, on one or more VGAM1877 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[62221] It is yet further appreciated that a function of VGAM1877 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1877 correlate with, and may be deduced from, the identity of the host target genes which VGAM1877 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62222] Nucleotide sequences of the VGAM1877 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1877 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1877 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1877 are further described hereinbelow with reference to Table 1.

[62223] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1877 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1877 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62224] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1877 gene, herein designated VGAM is inhibition of expression of VGAM1877 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1877 correlate with, and may be deduced from, the identity of the target genes which VGAM1877 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62225] A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248) is a VGAM1877 host target gene. AKAP11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP11 BINDING SITE, designated SEQ ID:18372, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62226] A function of VGAM1877 is therefore inhibition of A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession

NM\_016248). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP11. CG012 (Accession XM\_096710) is another VGAM1877 host target gene.

CG012 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CG012, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CG012 BINDING SITE, designated SEQ ID:40490, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62227] Another function of VGAM1877 is therefore inhibition of CG012 (Accession XM\_096710). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CG012. KIAA0565 (Accession XM\_039912) is another VGAM1877 host target gene. KIAA0565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA0565 BINDING SITE, designated SEQ ID:33222, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62228] Another function of VGAM1877 is therefore inhibition of KIAA0565 (Accession XM\_039912). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0565. Methionyl Aminopeptidase 1 (METAP1, Accession XM\_052334) is another VGAM1877 host target gene. METAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by METAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of METAP1 BINDING SITE, designated SEQ ID:35959, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62229] Another function of VGAM1877 is therefore inhibition of Methionyl Aminopeptidase 1 (METAP1, Accession XM\_052334). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with METAP1. PTD002 (Accession NM\_016144) is another VGAM1877 host target gene. PTD002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTD002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTD002 BINDING SITE, designated SEQ ID:18228, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62230] Another function of VGAM1877 is therefore inhibition of PTD002 (Accession NM\_016144). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTD002. RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM\_088733) is another VGAM1877 host target gene. RAB40A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB40A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB40A BINDING SITE, designated SEQ

ID:39928, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62231] Another function of VGAM1877 is therefore inhibition of RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM\_088733). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB40A. LOC146723 (Accession XM\_085565) is another VGAM1877 host target gene. LOC146723 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146723, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146723 BINDING SITE, designated SEQ ID:38228, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62232] Another function of VGAM1877 is therefore inhibition of LOC146723 (Accession XM\_085565). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146723. LOC147341 (Accession XM\_097223) is an-

other VGAM1877 host target gene. LOC147341 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147341, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147341 BINDING SITE, designated SEQ ID:40826, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62233] Another function of VGAM1877 is therefore inhibition of LOC147341 (Accession XM\_097223). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147341. LOC196528 (Accession XM\_113745) is another VGAM1877 host target gene. LOC196528 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196528, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196528 BINDING SITE, designated SEQ ID:42408, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62234] Another function of VGAM1877 is therefore inhibition of LOC196528 (Accession XM\_113745). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196528. LOC203276 (Accession XM\_117523) is another VGAM1877 host target gene. LOC203276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203276 BINDING SITE, designated SEQ ID:43491, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62235] Another function of VGAM1877 is therefore inhibition of LOC203276 (Accession XM\_117523). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203276. LOC203305 (Accession XM\_117529) is another VGAM1877 host target gene. LOC203305 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203305, corresponding to a HOST TARGET binding site such as BIND-



ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203305 BINDING SITE, designated SEQ ID:43515, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62236] Another function of VGAM1877 is therefore inhibition of LOC203305 (Accession XM\_117529). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203305. LOC221662 (Accession XM\_166466) is another VGAM1877 host target gene. LOC221662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221662 BINDING SITE, designated SEQ ID:44391, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62237] Another function of VGAM1877 is therefore inhibition of LOC221662 (Accession XM\_166466). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221662. LOC254243 (Accession XM\_173233) is another VGAM1877 host target gene. LOC254243 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254243 BINDING SITE, designated SEQ ID:46517, to the nucleotide sequence of VGAM1877 RNA, herein designated VGAM RNA, also designated SEQ ID:4588.

[62238] Another function of VGAM1877 is therefore inhibition of LOC254243 (Accession XM\_173233). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254243. LOC90038 (Accession XM\_028305) is another VGAM1877 host target gene. LOC90038 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90038 BINDING SITE, designated SEQ ID:30654, to the nucleotide sequence of VGAM1877 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4588.

[62239] Another function of VGAM1877 is therefore inhibition of LOC90038 (Accession XM\_028305). Accordingly, utilities of VGAM1877 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90038. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1878 (VGAM1878) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62240] VGAM1878 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1878 was detected is described hereinabove with reference to Figs. 1–8.

[62241] VGAM1878 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Respiratory Syncytial Virus. VGAM1878 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62242] VGAM1878 gene encodes a VGAM1878 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1878 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1878 precursor RNA is designated SEQ ID:1864, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1864 is located at position 7295 relative to the genome of Bovine Respiratory Syncytial Virus.

[62243] VGAM1878 precursor RNA folds onto itself, forming VGAM1878 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62244] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1878 folded precursor RNA into VGAM1878 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1878 RNA is designated SEQ ID:4589, and is provided hereinbelow with reference to the sequence listing part.

[62245] VGAM1878 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1878 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1878 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62246] VGAM1878 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1878 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1878 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1878 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1878 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[62247] The complementary binding of VGAM1878 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1878 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1878 host target RNA into VGAM1878 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62248] It is appreciated that VGAM1878 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1878 host target genes. The mRNA of

each one of this plurality of VGAM1878 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1878 RNA, herein designated VGAM RNA, and which when bound by VGAM1878 RNA causes inhibition of translation of respective one or more VGAM1878 host target proteins.

[62249] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1878 gene, herein designated VGAM GENE, on one or more VGAM1878 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[62250] It is yet further appreciated that a function of VGAM1878 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1878 include diagnosis, prevention and treatment of viral infection by Bovine Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1878 correlate with, and may be deduced from, the identity of the host target genes which VGAM1878 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62251] Nucleotide sequences of the VGAM1878 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1878 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1878 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1878 are further described hereinbelow with reference to Table 1.

[62252] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1878 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1878 RNA,



herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62253] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1878 gene, herein designated VGAM is inhibition of expression of VGAM1878 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1878 correlate with, and may be deduced from, the identity of the target genes which VGAM1878 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62254] DKFZp434J1015 (Accession XM\_166538) is a VGAM1878 host target gene. DKFZp434J1015 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434J1015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434J1015 BINDING SITE, designated SEQ ID:44505, to the nucleotide sequence of VGAM1878 RNA, herein designated VGAM RNA, also designated SEQ ID:4589.

[62255] A function of VGAM1878 is therefore inhibition of DKFZp434J1015 (Accession XM\_166538). Accordingly, utilities of VGAM1878 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZp434J1015. Formin Homology 2 Domain Containing 2 (FHOD2, Accession XM\_057927) is another VGAM1878 host target gene. FHOD2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FHOD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHOD2 BINDING SITE, designated SEQ ID:36554, to the nucleotide sequence of VGAM1878 RNA, herein designated VGAM RNA, also designated SEQ ID:4589.

[62256] Another function of VGAM1878 is therefore inhibition of Formin Homology 2 Domain Containing 2 (FHOD2, Accession XM\_057927). Accordingly, utilities of VGAM1878 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHOD2. FLJ32784 (Accession NM\_144623) is another VGAM1878 host target gene. FLJ32784 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ32784, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of FLJ32784 BINDING SITE, designated SEQ ID:29441, to the nucleotide sequence of VGAM1878 RNA, herein designated VGAM RNA, also designated SEQ ID:4589.

[62257] Another function of VGAM1878 is therefore inhibition of FLJ32784 (Accession NM\_144623). Accordingly, utilities of VGAM1878 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32784. LOC146520 (Accession XM\_085492) is another VGAM1878 host target gene. LOC146520 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146520 BINDING SITE, designated SEQ ID:38184, to the nucleotide sequence of VGAM1878 RNA, herein designated VGAM RNA, also designated SEQ ID:4589.

[62258] Another function of VGAM1878 is therefore inhibition of LOC146520 (Accession XM\_085492). Accordingly, utilities of VGAM1878 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146520. LOC149711 (Accession XM\_097720) is an-

other VGAM1878 host target gene. LOC149711 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149711 BINDING SITE, designated SEQ ID:41073, to the nucleotide sequence of VGAM1878 RNA, herein designated VGAM RNA, also designated SEQ ID:4589.

[62259] Another function of VGAM1878 is therefore inhibition of LOC149711 (Accession XM\_097720). Accordingly, utilities of VGAM1878 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149711. LOC150113 (Accession XM\_104532) is another VGAM1878 host target gene. LOC150113 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150113 BINDING SITE, designated SEQ ID:42170, to the nucleotide sequence of VGAM1878 RNA, herein designated VGAM RNA, also designated SEQ ID:4589.

[62260] Another function of VGAM1878 is therefore inhibition of LOC150113 (Accession XM\_104532). Accordingly, utilities of VGAM1878 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150113. LOC90288 (Accession XM\_030669) is another VGAM1878 host target gene. LOC90288 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90288, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90288 BINDING SITE, designated SEQ ID:31115, to the nucleotide sequence of VGAM1878 RNA, herein designated VGAM RNA, also designated SEQ ID:4589.

[62261] Another function of VGAM1878 is therefore inhibition of LOC90288 (Accession XM\_030669). Accordingly, utilities of VGAM1878 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90288. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1879 (VGAM1879) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[62262] VGAM1879 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1879 was detected is described hereinabove with reference to Figs. 1–8.

[62263] VGAM1879 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Respiratory Syncytial Virus. VGAM1879 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62264] VGAM1879 gene encodes a VGAM1879 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1879 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1879 precursor RNA is designated SEQ ID:1865, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1865 is located at position 5455 relative to the genome of Bovine Respiratory Syncytial Virus.

[62265] VGAM1879 precursor RNA folds onto itself, forming VGAM1879 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62266] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1879 folded precursor RNA into VGAM1879 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM1879 RNA is designated SEQ ID:4590, and is provided hereinbelow with reference to the sequence listing part.

[62267] VGAM1879 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1879 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1879 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62268] VGAM1879 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1879 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1879 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1879 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1879 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in



the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62269] The complementary binding of VGAM1879 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1879 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1879 host target RNA into VGAM1879 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62270] It is appreciated that VGAM1879 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1879 host target genes. The mRNA of each one of this plurality of VGAM1879 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1879 RNA, herein designated VGAM RNA, and which when bound by VGAM1879 RNA causes inhibition of translation of respective one or more VGAM1879 host target proteins.

[62271] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1879 gene, herein designated VGAM GENE, on one or more VGAM1879 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62272] It is yet further appreciated that a function of VGAM1879 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1879 include diagnosis, prevention and treatment of viral infection by Bovine Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1879 correlate with, and may be deduced from, the identity of the host target genes which VGAM1879 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[62273] Nucleotide sequences of the VGAM1879 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1879 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1879 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1879 are further described hereinbelow with reference to Table 1.

[62274] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1879 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1879 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62275] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1879 gene, herein designated VGAM is inhibition of expression of VGAM1879 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1879 correlate with, and may be deduced from, the identity of the target genes which VGAM1879 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62276] Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 12 (PSMD12, Accession NM\_002816) is a VGAM1879 host target gene. PSMD12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMD12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMD12 BINDING SITE, designated SEQ ID:8682, to the nucleotide sequence of VGAM1879 RNA, herein designated VGAM RNA, also designated SEQ ID:4590.

[62277] A function of VGAM1879 is therefore inhibition of Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 12 (PSMD12, Accession NM\_002816). Accordingly, utilities of VGAM1879 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMD12. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1880 (VGAM1880) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62278] VGAM1880 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1880 was detected is described hereinabove with reference to Figs. 1-8.

[62279] VGAM1880 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Respiratory Syncytial Virus. VGAM1880 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62280] VGAM1880 gene encodes a VGAM1880 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1880 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1880 precursor RNA is designated SEQ ID:1866, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1866 is located at position 14933 relative to the genome of Bovine Respiratory Syncytial Virus.

[62281] VGAM1880 precursor RNA folds onto itself, forming VGAM1880 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62282] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1880 folded precursor RNA into VGAM1880 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1880 RNA is designated SEQ ID:4591, and is provided hereinbelow with reference to the sequence listing part.

[62283] VGAM1880 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1880 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1880 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[62284] VGAM1880 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1880 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1880 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1880 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1880 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62285] The complementary binding of VGAM1880 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1880 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1880 host target RNA into VGAM1880 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62286] It is appreciated that VGAM1880 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1880 host target genes. The mRNA of each one of this plurality of VGAM1880 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1880 RNA, herein designated VGAM RNA, and which when bound by VGAM1880 RNA causes inhibition of translation of respective one or more VGAM1880 host target proteins.

[62287] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1880 gene, herein designated VGAM GENE, on one or more VGAM1880 host target gene, herein designated



VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62288] It is yet further appreciated that a function of VGAM1880 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1880 include diagnosis, prevention and treatment of viral infection by Bovine Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1880 correlate with, and may be deduced from, the identity of the host target genes which VGAM1880 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62289] Nucleotide sequences of the VGAM1880 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1880 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1880 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1880 are further  
described hereinbelow with reference to Table 1.

[62290] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1880 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1880 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[62291] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1880 gene, herein designated VGAM is  
inhibition of expression of VGAM1880 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1880 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1880  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[62292] Cytochrome P450, Subfamily I (aromatic compound-in-  
ducible), Polypeptide 1 (CYP1A1, Accession NM\_000499)

is a VGAM1880 host target gene. CYP1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP1A1 BINDING SITE, designated SEQ ID:6113, to the nucleotide sequence of VGAM1880 RNA, herein designated VGAM RNA, also designated SEQ ID:4591.

[62293] A function of VGAM1880 is therefore inhibition of Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 1 (CYP1A1, Accession NM\_000499), a gene which intervenes in an NADPH-dependent electron transport pathway. Accordingly, utilities of VGAM1880 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP1A1. The function of CYP1A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM335.FLJ10781 (Accession NM\_018215) is another VGAM1880 host target gene. FLJ10781 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10781, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10781 BINDING SITE, designated SEQ ID:20132, to the nucleotide sequence of VGAM1880 RNA, herein designated VGAM RNA, also designated SEQ ID:4591.

[62294] Another function of VGAM1880 is therefore inhibition of FLJ10781 (Accession NM\_018215). Accordingly, utilities of VGAM1880 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10781. LOC51580 (Accession NM\_015874) is another VGAM1880 host target gene. LOC51580 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51580 BINDING SITE, designated SEQ ID:18013, to the nucleotide sequence of VGAM1880 RNA, herein designated VGAM RNA, also designated SEQ ID:4591.

[62295] Another function of VGAM1880 is therefore inhibition of LOC51580 (Accession NM\_015874). Accordingly, utilities of VGAM1880 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC51580. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1881 (VGAM1881) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62296] VGAM1881 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1881 was detected is described hereinabove with reference to Figs. 1–8.

[62297] VGAM1881 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Respiratory Syncytial Virus. VGAM1881 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62298] VGAM1881 gene encodes a VGAM1881 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1881 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1881 precursor RNA is desig-

nated SEQ ID:1867, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1867 is located at position 7527 relative to the genome of Bovine Respiratory Syncytial Virus.

- [62299] VGAM1881 precursor RNA folds onto itself, forming VGAM1881 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [62300] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1881 folded precursor RNA into VGAM1881 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1881 RNA is designated SEQ ID:4592, and is provided hereinbelow with reference to the sequence

listing part.

[62301] VGAM1881 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1881 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1881 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62302] VGAM1881 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1881 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1881 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1881 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1881 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62303] The complementary binding of VGAM1881 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1881 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1881 host target RNA into VGAM1881 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62304] It is appreciated that VGAM1881 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1881 host target genes. The mRNA of each one of this plurality of VGAM1881 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1881 RNA, herein designated VGAM



RNA, and which when bound by VGAM1881 RNA causes inhibition of translation of respective one or more VGAM1881 host target proteins.

[62305] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1881 gene, herein designated VGAM GENE, on one or more VGAM1881 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62306] It is yet further appreciated that a function of VGAM1881 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1881 include diagnosis, prevention and treatment of viral infection by Bovine Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1881 correlate with, and may be deduced from, the identity of the host target genes which VGAM1881 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62307] Nucleotide sequences of the VGAM1881 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1881 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1881 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1881 are further described hereinbelow with reference to Table 1.

[62308] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1881 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1881 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62309] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1881 gene, herein designated VGAM is

inhibition of expression of VGAM1881 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1881 correlate with, and may be deduced from, the identity of the target genes which VGAM1881 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62310] Hepatic Leukemia Factor (HLF, Accession NM\_002126) is a VGAM1881 host target gene. HLF BINDING SITE1 and HLF BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HLF, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HLF BINDING SITE1 and HLF BINDING SITE2, designated SEQ ID:7900 and SEQ ID:7901 respectively, to the nucleotide sequence of VGAM1881 RNA, herein designated VGAM RNA, also designated SEQ ID:4592.

[62311] A function of VGAM1881 is therefore inhibition of Hepatic Leukemia Factor (HLF, Accession NM\_002126). Accordingly, utilities of VGAM1881 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HLF. KIAA0594 (Accession XM\_036117) is another VGAM1881 host target gene. KIAA0594 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0594, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0594 BINDING SITE, designated SEQ ID:32389, to the nucleotide sequence of VGAM1881 RNA, herein designated VGAM RNA, also designated SEQ ID:4592.

[62312] Another function of VGAM1881 is therefore inhibition of KIAA0594 (Accession XM\_036117). Accordingly, utilities of VGAM1881 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0594. KIAA1040 (Accession XM\_051091) is another VGAM1881 host target gene. KIAA1040 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1040 BINDING SITE, designated SEQ ID:35736, to the nucleotide sequence of VGAM1881 RNA, herein designated VGAM RNA, also designated SEQ ID:4592.

[62313] Another function of VGAM1881 is therefore inhibition of

KIAA1040 (Accession XM\_051091). Accordingly, utilities of VGAM1881 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1040. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1882 (VGAM1882) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62314] VGAM1882 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1882 was detected is described hereinabove with reference to Figs. 1-8.

[62315] VGAM1882 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Respiratory Syncytial Virus. VGAM1882 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62316] VGAM1882 gene encodes a VGAM1882 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1882 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1882 precursor RNA is designated SEQ ID:1868, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1868 is located at position 417 relative to the genome of Bovine Respiratory Syncytial Virus.

- [62317] VGAM1882 precursor RNA folds onto itself, forming VGAM1882 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [62318] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1882 folded precursor RNA into VGAM1882 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide se-

quence of VGAM1882 RNA is designated SEQ ID:4593, and is provided hereinbelow with reference to the sequence listing part.

[62319] VGAM1882 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1882 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1882 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62320] VGAM1882 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1882 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1882 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1882 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1882 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62321] The complementary binding of VGAM1882 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1882 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1882 host target RNA into VGAM1882 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62322] It is appreciated that VGAM1882 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1882 host target genes. The mRNA of each one of this plurality of VGAM1882 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1882 RNA, herein designated VGAM RNA, and which when bound by VGAM1882 RNA causes inhibition of translation of respective one or more VGAM1882 host target proteins.

[62323] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1882 gene, herein designated VGAM GENE, on one or more VGAM1882 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62324] It is yet further appreciated that a function of VGAM1882

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1882 include diagnosis, prevention and treatment of viral infection by Bovine Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1882 correlate with, and may be deduced from, the identity of the host target genes which VGAM1882 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62325] Nucleotide sequences of the VGAM1882 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1882 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1882 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1882 are further described hereinbelow with reference to Table 1.

[62326] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1882 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1882 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62327] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1882 gene, herein designated VGAM is inhibition of expression of VGAM1882 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1882 correlate with, and may be deduced from, the identity of the target genes which VGAM1882 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62328] Caveolin 1, Caveolae Protein, 22kDa (CAV1, Accession NM\_001753) is a VGAM1882 host target gene. CAV1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAV1 BINDING SITE, designated SEQ ID:7490, to the nucleotide sequence of VGAM1882 RNA, herein designated VGAM RNA, also designated SEQ ID:4593.

[62329] A function of VGAM1882 is therefore inhibition of Caveolin 1, Caveolae Protein, 22kDa (CAV1, Accession NM\_001753), a gene which may act as a scaffolding protein within caveolar membranes, and interacts directly with g-protein alpha subunits and can functionally regu-

late their activity. Accordingly, utilities of VGAM1882 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAV1. The function of CAV1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM331.FLJ30294 (Accession NM\_144632) is another VGAM1882 host target gene. FLJ30294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30294 BINDING SITE, designated SEQ ID:29452, to the nucleotide sequence of VGAM1882 RNA, herein designated VGAM RNA, also designated SEQ ID:4593.

[62330] Another function of VGAM1882 is therefore inhibition of FLJ30294 (Accession NM\_144632). Accordingly, utilities of VGAM1882 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30294. KIAA1571 (Accession XM\_027744) is another VGAM1882 host target gene. KIAA1571 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1571, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1571 BINDING SITE, designated SEQ ID:30567, to the nucleotide sequence of VGAM1882 RNA, herein designated VGAM RNA, also designated SEQ ID:4593.

[62331] Another function of VGAM1882 is therefore inhibition of KIAA1571 (Accession XM\_027744). Accordingly, utilities of VGAM1882 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1571. LOC201965 (Accession XM\_114412) is another VGAM1882 host target gene. LOC201965 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201965, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201965 BINDING SITE, designated SEQ ID:42931, to the nucleotide sequence of VGAM1882 RNA, herein designated VGAM RNA, also designated SEQ ID:4593.

[62332] Another function of VGAM1882 is therefore inhibition of LOC201965 (Accession XM\_114412). Accordingly, utilities

of VGAM1882 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201965. LOC257017 (Accession XM\_173227) is another VGAM1882 host target gene. LOC257017 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257017 BINDING SITE, designated SEQ ID:46494, to the nucleotide sequence of VGAM1882 RNA, herein designated VGAM RNA, also designated SEQ ID:4593.

[62333] Another function of VGAM1882 is therefore inhibition of LOC257017 (Accession XM\_173227). Accordingly, utilities of VGAM1882 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257017. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1883 (VGAM1883) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62334] VGAM1883 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1883 was detected is described hereinabove with reference to Figs. 1-8.

[62335] VGAM1883 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Respiratory Syncytial Virus. VGAM1883 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62336] VGAM1883 gene encodes a VGAM1883 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1883 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1883 precursor RNA is designated SEQ ID:1869, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1869 is located at position 10923 relative to the genome of Bovine Respiratory Syncytial Virus.

[62337] VGAM1883 precursor RNA folds onto itself, forming VGAM1883 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62338] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1883 folded precursor RNA into VGAM1883 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1883 RNA is designated SEQ ID:4594, and is provided hereinbelow with reference to the sequence listing part.

[62339] VGAM1883 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1883 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1883 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated



5`UTR, PROTEIN CODING and 3`UTR respectively.

[62340] VGAM1883 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1883 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1883 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1883 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1883 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62341] The complementary binding of VGAM1883 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1883 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1883 host target RNA into VGAM1883 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62342] It is appreciated that VGAM1883 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1883 host target genes. The mRNA of each one of this plurality of VGAM1883 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1883 RNA, herein designated VGAM RNA, and which when bound by VGAM1883 RNA causes inhibition of translation of respective one or more VGAM1883 host target proteins.

[62343] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1883 gene, herein designated VGAM GENE, on one or more VGAM1883 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62344] It is yet further appreciated that a function of VGAM1883 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of viral infection by Bovine Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1883 correlate with, and may be deduced from, the identity of the host target genes which VGAM1883 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62345] Nucleotide sequences of the VGAM1883 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1883 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1883 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1883 are further  
described hereinbelow with reference to Table 1.

[62346] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1883 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1883 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[62347] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1883 gene, herein designated VGAM is  
inhibition of expression of VGAM1883 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1883 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1883  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[62348] Glutaminase (GLS, Accession NM\_014905) is a VGAM1883  
host target gene. GLS BINDING SITE is HOST TARGET bind-

ing site found in the 3` untranslated region of mRNA encoded by GLS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLS BINDING SITE, designated SEQ ID:17109, to the nucleotide sequence of VGAM1883 RNA, herein designated VGAM RNA, also designated SEQ ID:4594.

[62349] A function of VGAM1883 is therefore inhibition of Glutaminase (GLS, Accession NM\_014905). Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLS. Matrix Metalloproteinase 8 (neutrophil collagenase) (MMP8, Accession NM\_002424) is another VGAM1883 host target gene. MMP8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MMP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP8 BINDING SITE, designated SEQ ID:8257, to the nucleotide sequence of VGAM1883 RNA, herein designated VGAM RNA, also designated SEQ ID:4594.

[62350] Another function of VGAM1883 is therefore inhibition of Matrix Metalloproteinase 8 (neutrophil collagenase) (MMP8, Accession NM\_002424). Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP8. Selectin L (lymphocyte adhesion molecule 1) (SELL, Accession NM\_000655) is another VGAM1883 host target gene. SELL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SELL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SELL BINDING SITE, designated SEQ ID:6314, to the nucleotide sequence of VGAM1883 RNA, herein designated VGAM RNA, also designated SEQ ID:4594.

[62351] Another function of VGAM1883 is therefore inhibition of Selectin L (lymphocyte adhesion molecule 1) (SELL, Accession NM\_000655), a gene which is a cell surface adhesion protein. Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SELL. The function of SELL and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM374.DKFZP564D206 (Accession XM\_166501) is another VGAM1883 host target gene. DKFZP564D206 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564D206, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564D206 BINDING SITE, designated SEQ ID:44427, to the nucleotide sequence of VGAM1883 RNA, herein designated VGAM RNA, also designated SEQ ID:4594.

[62352] Another function of VGAM1883 is therefore inhibition of DKFZP564D206 (Accession XM\_166501). Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D206. DKFZP564I0422 (Accession NM\_031435) is another VGAM1883 host target gene. DKFZP564I0422 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564I0422, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of DKFZP564I0422 BINDING SITE, designated SEQ ID:25433, to the nucleotide sequence of VGAM1883 RNA, herein designated VGAM RNA, also designated SEQ ID:4594.

[62353] Another function of VGAM1883 is therefore inhibition of DKFZP564I0422 (Accession NM\_031435). Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I0422. FLJ23189 (Accession NM\_025057) is another VGAM1883 host target gene. FLJ23189 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23189 BINDING SITE, designated SEQ ID:24655, to the nucleotide sequence of VGAM1883 RNA, herein designated VGAM RNA, also designated SEQ ID:4594.

[62354] Another function of VGAM1883 is therefore inhibition of FLJ23189 (Accession NM\_025057). Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23189. P37NB (Accession NM\_005824) is another



VGAM1883 host target gene. P37NB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P37NB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P37NB BINDING SITE, designated SEQ ID:12433, to the nucleotide sequence of VGAM1883 RNA, herein designated VGAM RNA, also designated SEQ ID:4594.

[62355] Another function of VGAM1883 is therefore inhibition of P37NB (Accession NM\_005824). Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P37NB. Vesicular Membrane Protein P24 (VMP, Accession NM\_080723) is another VGAM1883 host target gene. VMP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VMP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VMP BINDING SITE, designated SEQ ID:28016, to the nucleotide sequence of VGAM1883 RNA, herein designated VGAM RNA, also designated SEQ ID:4594.

[62356] Another function of VGAM1883 is therefore inhibition of Vesicular Membrane Protein P24 (VMP, Accession NM\_080723). Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VMP. LOC170063 (Accession XM\_104820) is another VGAM1883 host target gene. LOC170063 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170063, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170063 BINDING SITE, designated SEQ ID:42187, to the nucleotide sequence of VGAM1883 RNA, herein designated VGAM RNA, also designated SEQ ID:4594.

[62357] Another function of VGAM1883 is therefore inhibition of LOC170063 (Accession XM\_104820). Accordingly, utilities of VGAM1883 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170063. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1884 (VGAM1884) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62358] VGAM1884 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1884 was detected is described hereinabove with reference to Figs. 1–8.

[62359] VGAM1884 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Respiratory Syncytial Virus. VGAM1884 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62360] VGAM1884 gene encodes a VGAM1884 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1884 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1884 precursor RNA is designated SEQ ID:1870, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1870 is located at position 8134 relative to the genome of Bovine Respiratory Syncytial Virus.

[62361] VGAM1884 precursor RNA folds onto itself, forming

VGAM1884 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62362] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1884 folded precursor RNA into VGAM1884 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1884 RNA is designated SEQ ID:4595, and is provided hereinbelow with reference to the sequence listing part.

[62363] VGAM1884 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1884 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1884 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62364] VGAM1884 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1884 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1884 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1884 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1884 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62365] The complementary binding of VGAM1884 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1884 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1884 host target RNA into VGAM1884 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62366] It is appreciated that VGAM1884 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1884 host target genes. The mRNA of each one of this plurality of VGAM1884 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1884 RNA, herein designated VGAM RNA, and which when bound by VGAM1884 RNA causes inhibition of translation of respective one or more VGAM1884 host target proteins.

[62367] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1884 gene, herein designated VGAM GENE, on one or more VGAM1884 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62368] It is yet further appreciated that a function of VGAM1884 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1884 include diagnosis, prevention and treatment of viral infection by Bovine Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1884 correlate with, and may be deduced from, the identity of the host target genes which VGAM1884 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62369] Nucleotide sequences of the VGAM1884 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1884 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1884 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1884 are further described hereinbelow with reference to Table 1.

[62370] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1884 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1884 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62371] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1884 gene, herein designated VGAM is inhibition of expression of VGAM1884 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1884 correlate with, and may be deduced from, the identity of the target genes which VGAM1884 binds and inhibits, and the function of these target genes,



as elaborated hereinbelow.

[62372] 5-methyltetrahydrofolate-homocysteine Methyltransferase Reductase (MTRR, Accession NM\_024010) is a VGAM1884 host target gene. MTRR BINDING SITE1 and MTRR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MTRR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTRR BINDING SITE1 and MTRR BINDING SITE2, designated SEQ ID:23444 and SEQ ID:8290 respectively, to the nucleotide sequence of VGAM1884 RNA, herein designated VGAM RNA, also designated SEQ ID:4595.

[62373] A function of VGAM1884 is therefore inhibition of 5-methyltetrahydrofolate-homocysteine Methyltransferase Reductase (MTRR, Accession NM\_024010). Accordingly, utilities of VGAM1884 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTRR. Protein Kinase, CAMP-dependent, Regulatory, Type I, Alpha (tissue specific extinguisher 1) (PRKAR1A, Accession NM\_002734) is another VGAM1884 host target gene. PRKAR1A BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by PRKAR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAR1A BINDING SITE, designated SEQ ID:8605, to the nucleotide sequence of VGAM1884 RNA, herein designated VGAM RNA, also designated SEQ ID:4595.

[62374] Another function of VGAM1884 is therefore inhibition of Protein Kinase, CAMP-dependent, Regulatory, Type I, Alpha (tissue specific extinguisher 1) (PRKAR1A, Accession NM\_002734). Accordingly, utilities of VGAM1884 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAR1A. Protein Kinase C, Nu (PRKCN, Accession NM\_005813) is another VGAM1884 host target gene. PRKCN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKCN BINDING SITE, designated SEQ ID:12395, to the nucleotide sequence of VGAM1884 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4595.

[62375] Another function of VGAM1884 is therefore inhibition of Protein Kinase C,  $\alpha$  (PRKCN, Accession NM\_005813). Accordingly, utilities of VGAM1884 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKCN. RINZF (Accession NM\_023929) is another VGAM1884 host target gene. RINZF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RINZF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RINZF BINDING SITE, designated SEQ ID:23411, to the nucleotide sequence of VGAM1884 RNA, herein designated VGAM RNA, also designated SEQ ID:4595.

[62376] Another function of VGAM1884 is therefore inhibition of RINZF (Accession NM\_023929). Accordingly, utilities of VGAM1884 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RINZF. LOC143692 (Accession XM\_084601) is another VGAM1884 host target gene. LOC143692 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143692, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143692 BINDING SITE, designated SEQ ID:37630, to the nucleotide sequence of VGAM1884 RNA, herein designated VGAM RNA, also designated SEQ ID:4595.

[62377] Another function of VGAM1884 is therefore inhibition of LOC143692 (Accession XM\_084601). Accordingly, utilities of VGAM1884 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143692. LOC158549 (Accession XM\_098963) is another VGAM1884 host target gene. LOC158549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158549 BINDING SITE, designated SEQ ID:42004, to the nucleotide sequence of VGAM1884 RNA, herein designated VGAM RNA, also designated SEQ ID:4595.

[62378] Another function of VGAM1884 is therefore inhibition of LOC158549 (Accession XM\_098963). Accordingly, utilities of VGAM1884 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC158549. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1885 (VGAM1885) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62379] VGAM1885 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1885 was detected is described hereinabove with reference to Figs. 1–8.

[62380] VGAM1885 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Newcastle Disease Virus. VGAM1885 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62381] VGAM1885 gene encodes a VGAM1885 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1885 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1885 precursor RNA is desig-

nated SEQ ID:1871, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1871 is located at position 363 relative to the genome of Newcastle Disease Virus.

- [62382] VGAM1885 precursor RNA folds onto itself, forming VGAM1885 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [62383] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1885 folded precursor RNA into VGAM1885 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1885 RNA is designated SEQ ID:4596, and is provided hereinbelow with reference to the sequence

listing part.

[62384] VGAM1885 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1885 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1885 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62385] VGAM1885 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1885 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1885 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1885 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1885 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62386] The complementary binding of VGAM1885 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1885 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1885 host target RNA into VGAM1885 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62387] It is appreciated that VGAM1885 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1885 host target genes. The mRNA of each one of this plurality of VGAM1885 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1885 RNA, herein designated VGAM



RNA, and which when bound by VGAM1885 RNA causes inhibition of translation of respective one or more VGAM1885 host target proteins.

[62388] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1885 gene, herein designated VGAM GENE, on one or more VGAM1885 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62389] It is yet further appreciated that a function of VGAM1885 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1885 include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGAM1885 correlate with, and may be deduced from, the identity of the host target genes which VGAM1885 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62390] Nucleotide sequences of the VGAM1885 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1885 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1885 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1885 are further described hereinbelow with reference to Table 1.

[62391] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1885 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1885 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62392] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1885 gene, herein designated VGAM is

inhibition of expression of VGAM1885 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1885 correlate with, and may be deduced from, the identity of the target genes which VGAM1885 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62393] B-cell CLL/lymphoma 11A (zinc finger protein) (BCL11A, Accession NM\_138553) is a VGAM1885 host target gene. BCL11A BINDING SITE1 and BCL11A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BCL11A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL11A BINDING SITE1 and BCL11A BINDING SITE2, designated SEQ ID:28851 and SEQ ID:19751 respectively, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62394] A function of VGAM1885 is therefore inhibition of B-cell CLL/lymphoma 11A (zinc finger protein) (BCL11A, Accession NM\_138553), a gene which acts as a transcriptional repressor. Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with BCL11A. The function of BCL11A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM190.BTG Family, Member 2 (BTG2, Accession NM\_006763) is another VGAM1885 host target gene. BTG2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BTG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTG2 BINDING SITE, designated SEQ ID:13620, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62395] Another function of VGAM1885 is therefore inhibition of BTG Family, Member 2 (BTG2, Accession NM\_006763). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTG2. Cadherin, EGF LAG Seven-pass G-type Receptor 2 (flamingo homolog, Drosophila) (CELSR2, Accession NM\_001408) is another VGAM1885 host target gene. CELSR2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

CELSR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CELSR2 BINDING SITE, designated SEQ ID:7108, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62396] Another function of VGAM1885 is therefore inhibition of Cadherin, EGF LAG Seven-pass G-type Receptor 2 (flamingo homolog, Drosophila) (CELSR2, Accession NM\_001408), a gene which is a calcium dependent cell adhesion protein. Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CELSR2. The function of CELSR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM432. Centrin, EF-hand Protein, 1 (CETN1, Accession XM\_170866) is another VGAM1885 host target gene. CETN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CETN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of CETN1 BINDING SITE, designated SEQ ID:45639, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62397] Another function of VGAM1885 is therefore inhibition of Centrin, EF-hand Protein, 1 (CETN1, Accession XM\_170866). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CETN1. LIM Domain Only 4 (LMO4, Accession NM\_006769) is another VGAM1885 host target gene. LMO4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LMO4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMO4 BINDING SITE, designated SEQ ID:13643, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62398] Another function of VGAM1885 is therefore inhibition of LIM Domain Only 4 (LMO4, Accession NM\_006769), a gene which promotes myogenic differentiation. Accordingly,

utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMO4. The function of LMO4 has been established by previous studies. Muscle development is a complex, multistep process under the control of both ubiquitous and muscle-specific transcriptional regulators. Arber et al. (1994) described a positive regulator of myogenesis that was cloned from a subtracted cDNA library enriched for messages induced in denervated rat skeletal muscle. The rat cDNA was designated muscle LIM protein (Mlp) because it contained a cysteine-rich domain originally described in the 3 proteins Lin-11, Isl-1 (OMIM Ref. No. 600366), and Mec-3. Mlp is enriched in striated muscle and its expression coincides with myogenic differentiation. In the absence of Mlp, induced myoblasts express myogenin but fail to exit the cell cycle and differentiate. The rat Mlp cDNA encodes a predicted 194-amino acid protein containing 2 LIM motifs. The protein is highly conserved and Northern blots detected transcripts in chicken and Drosophila, from which the corresponding genes were isolated. The chicken and rat proteins are 93% identical. Fung et al. (1995) cloned a human cDNA, which they designated cardiac LIM protein (CLP), whose deduced

amino acid sequence is 95% identical to that of rat Mlp. The authors proposed that the human gene is the homolog of the rat sequence. Northern blots showed expression in cardiac and slow-twitch skeletal muscles

[62399] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[62400] Arber, S.; Halder, G.; Caroni, P. : Muscle LIM protein, a novel essential regulator of myogenesis, promotes myogenic differentiation. *Cell* 79: 221-231, 1994. ; and

[62401] Weiskirchen, R.; Pino, J. D.; Macalma, T.; Bister, K.; Beckerle, M. C. : The cysteine-rich protein family of highly related LIM domain proteins. *J. Biol. Chem.* 270: 28946-28954, 1995.

[62402] Further studies establishing the function and utilities of LMO4 are found in John Hopkins OMIM database record ID 600824, and in cited publications numbered 7775-777 and 3980 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mitogen-activated Protein Kinase Kinase Kinase 1 (MAP3K1, Accession XM\_042066) is another VGAM1885 host target gene. MAP3K1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA



encoded by MAP3K1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K1 BINDING SITE, designated SEQ ID:33680, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62403] Another function of VGAM1885 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 1 (MAP3K1, Accession XM\_042066), a gene which can phosphorylate and activate mapkk 1 and mapkk 2 (mek1/mek2) which leads to phosphorylation of map kinases. it is also a highly efficient activator of the jnk cascade. Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K1. The function of MAP3K1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM469. MAX Binding Protein (MNT, Accession NM\_020310) is another VGAM1885 host target gene. MNT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MNT, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MNT BINDING SITE, designated SEQ ID:21566, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62404] Another function of VGAM1885 is therefore inhibition of MAX Binding Protein (MNT, Accession NM\_020310). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MNT. Membrane Protein, Palmitoylated 5 (MAGUK p55 subfamily member 5) (MPP5, Accession NM\_022474) is another VGAM1885 host target gene. MPP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPP5 BINDING SITE, designated SEQ ID:22839, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62405] Another function of VGAM1885 is therefore inhibition of Membrane Protein, Palmitoylated 5 (MAGUK p55 subfamily

member 5) (MPP5, Accession NM\_022474), a gene which may regulate transmembrane proteins that bind calcium, calmodulin, or nucleotides. Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPP5. The function of MPP5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM306. Aminopeptidase Puromycin Sensitive (NPEPPS, Accession NM\_006310) is another VGAM1885 host target gene. NPEPPS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPEPPS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPEPPS BINDING SITE, designated SEQ ID:12999, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62406] Another function of VGAM1885 is therefore inhibition of Aminopeptidase Puromycin Sensitive (NPEPPS, Accession NM\_006310), a gene which is puromycin-sensitive aminopeptidase and has metallopeptidase activity. Ac-

cordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPEPPS. The function of NPEPPS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM83. RNTRE (Accession NM\_014688) is another VGAM1885 host target gene. RNTRE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNTRE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNTRE BINDING SITE, designated SEQ ID:16188, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62407] Another function of VGAM1885 is therefore inhibition of RNTRE (Accession NM\_014688), a gene which may be involved in cell proliferation. Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNTRE. The function of RNTRE and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM379.Sodium Channel, Voltage-gated, Type III, Alpha Polypeptide (SCN3A, Accession NM\_006922) is another VGAM1885 host target gene. SCN3A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SCN3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN3A BINDING SITE, designated SEQ ID:13795, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62408] Another function of VGAM1885 is therefore inhibition of Sodium Channel, Voltage-gated, Type III, Alpha Polypeptide (SCN3A, Accession NM\_006922), a gene which may be important for maintaining neural membrane excitability. Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN3A. The function of SCN3A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM124.Solute Carrier Family 4, Sodium Bicarbonate Cotransporter,

Member 4 (SLC4A4, Accession NM\_003759) is another VGAM1885 host target gene. SLC4A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC4A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A4 BINDING SITE, designated SEQ ID:9837, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62409] Another function of VGAM1885 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 4 (SLC4A4, Accession NM\_003759), a gene which is a sodium bicarbonate cotransporter. Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A4. The function of SLC4A4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM222. Sorbin and SH3 Domain Containing 1 (SORBS1, Accession NM\_015385) is another VGAM1885 host target gene. SORBS1 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by SORBS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORBS1 BINDING SITE, designated SEQ ID:17687, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62410] Another function of VGAM1885 is therefore inhibition of Sorbin and SH3 Domain Containing 1 (SORBS1, Accession NM\_015385), a gene which necessary for cell polarization during vegetative growth. Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORBS1. The function of SORBS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM475. Tissue Inhibitor of Metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory) (TIMP3, Accession NM\_000362) is another VGAM1885 host target gene. TIMP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIMP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIMP3 BINDING SITE, designated SEQ ID:5932, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62411] Another function of VGAM1885 is therefore inhibition of Tissue Inhibitor of Metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory) (TIMP3, Accession NM\_000362). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIMP3. CMG2 (Accession NM\_058172) is another VGAM1885 host target gene. CMG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CMG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CMG2 BINDING SITE, designated SEQ ID:27719, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62412] Another function of VGAM1885 is therefore inhibition of CMG2 (Accession NM\_058172). Accordingly, utilities of



VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CMG2. DnaJ (Hsp40) Homolog, Subfamily C, Member 6 (DNAJC6, Accession NM\_014787) is another VGAM1885 host target gene. DNAJC6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DNAJC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJC6 BINDING SITE, designated SEQ ID:16662, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62413] Another function of VGAM1885 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily C, Member 6 (DNAJC6, Accession NM\_014787). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJC6. FLJ20291 (Accession NM\_017748) is another VGAM1885 host target gene. FLJ20291 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20291, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20291 BINDING SITE, designated SEQ ID:19342, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62414] Another function of VGAM1885 is therefore inhibition of FLJ20291 (Accession NM\_017748). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20291. FLJ21870 (Accession NM\_023016) is another VGAM1885 host target gene. FLJ21870 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21870 BINDING SITE, designated SEQ ID:23278, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62415] Another function of VGAM1885 is therefore inhibition of FLJ21870 (Accession NM\_023016). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ21870. IMP-2 (Accession NM\_006548) is another VGAM1885 host target gene. IMP-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IMP-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMP-2 BINDING SITE, designated SEQ ID:13306, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62416] Another function of VGAM1885 is therefore inhibition of IMP-2 (Accession NM\_006548). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMP-2. KIAA0628 (Accession NM\_014789) is another VGAM1885 host target gene. KIAA0628 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0628, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0628 BINDING SITE, designated SEQ ID:16675, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4596.

[62417] Another function of VGAM1885 is therefore inhibition of KIAA0628 (Accession NM\_014789). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0628. KIAA0737 (Accession NM\_014828) is another VGAM1885 host target gene. KIAA0737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0737 BINDING SITE, designated SEQ ID:16816, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62418] Another function of VGAM1885 is therefore inhibition of KIAA0737 (Accession NM\_014828). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0737. KIAA0820 (Accession XM\_044463) is another VGAM1885 host target gene. KIAA0820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0820, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0820 BINDING SITE, designated SEQ ID:34219, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62419] Another function of VGAM1885 is therefore inhibition of KIAA0820 (Accession XM\_044463). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0820. KIAA1128 (Accession XM\_043596) is another VGAM1885 host target gene. KIAA1128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1128 BINDING SITE, designated SEQ ID:33970, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62420] Another function of VGAM1885 is therefore inhibition of KIAA1128 (Accession XM\_043596). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1128. KIAA1450 (Accession XM\_038035) is another VGAM1885 host target gene. KIAA1450 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1450 BINDING SITE, designated SEQ ID:32747, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62421] Another function of VGAM1885 is therefore inhibition of KIAA1450 (Accession XM\_038035). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1450. KIAA1641 (Accession XM\_087167) is another VGAM1885 host target gene. KIAA1641 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1641, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1641 BINDING SITE, designated SEQ ID:39098, to the

nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62422] Another function of VGAM1885 is therefore inhibition of KIAA1641 (Accession XM\_087167). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1641. KIAA1713 (Accession XM\_051335) is another VGAM1885 host target gene. KIAA1713 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1713 BINDING SITE, designated SEQ ID:35810, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62423] Another function of VGAM1885 is therefore inhibition of KIAA1713 (Accession XM\_051335). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1713. KIAA1944 (Accession XM\_062545) is another VGAM1885 host target gene. KIAA1944 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1944, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1944 BINDING SITE, designated SEQ ID:37224, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62424] Another function of VGAM1885 is therefore inhibition of KIAA1944 (Accession XM\_062545). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1944. MGC26954 (Accession NM\_145025) is another VGAM1885 host target gene. MGC26954 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC26954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC26954 BINDING SITE, designated SEQ ID:29638, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62425] Another function of VGAM1885 is therefore inhibition of MGC26954 (Accession NM\_145025). Accordingly, utilities



of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC26954. Mitochondrial Ribosomal Protein 63 (MRP63, Accession NM\_024026) is another VGAM1885 host target gene. MRP63 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRP63, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRP63 BINDING SITE, designated SEQ ID:23455, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62426] Another function of VGAM1885 is therefore inhibition of Mitochondrial Ribosomal Protein 63 (MRP63, Accession NM\_024026). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRP63. Placenta-specific 3 (PLAC3, Accession XM\_045115) is another VGAM1885 host target gene. PLAC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLAC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAC3 BINDING SITE, designated SEQ ID:34367, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62427] Another function of VGAM1885 is therefore inhibition of Placenta-specific 3 (PLAC3, Accession XM\_045115). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAC3. Phospholipid Scramblase 2 (PLSCR2, Accession NM\_020359) is another VGAM1885 host target gene. PLSCR2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLSCR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLSCR2 BINDING SITE, designated SEQ ID:21631, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62428] Another function of VGAM1885 is therefore inhibition of Phospholipid Scramblase 2 (PLSCR2, Accession NM\_020359). Accordingly, utilities of VGAM1885 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with PLSCR2. PTD002 (Accession NM\_016144) is another VGAM1885 host target gene.

PTD002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTD002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTD002 BINDING SITE, designated SEQ ID:18229, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62429] Another function of VGAM1885 is therefore inhibition of PTD002 (Accession NM\_016144). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTD002. RAP140 (Accession NM\_015224) is another VGAM1885 host target gene. RAP140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP140

BINDING SITE, designated SEQ ID:17558, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62430] Another function of VGAM1885 is therefore inhibition of RAP140 (Accession NM\_015224). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAP140. RNO2 (Accession NM\_033297) is another VGAM1885 host target gene. RNO2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RNO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNO2 BINDING SITE, designated SEQ ID:27126, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62431] Another function of VGAM1885 is therefore inhibition of RNO2 (Accession NM\_033297). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNO2. TACTILE (Accession NM\_005816) is another VGAM1885 host target gene. TACTILE BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by TACTILE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TACTILE BINDING SITE, designated SEQ ID:12413, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62432] Another function of VGAM1885 is therefore inhibition of TACTILE (Accession NM\_005816). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TACTILE. LOC115073 (Accession XM\_055193) is another VGAM1885 host target gene. LOC115073 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115073 BINDING SITE, designated SEQ ID:36241, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62433] Another function of VGAM1885 is therefore inhibition of

LOC115073 (Accession XM\_055193). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115073. LOC116123 (Accession NM\_138784) is another VGAM1885 host target gene. LOC116123 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC116123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116123 BINDING SITE, designated SEQ ID:29013, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62434] Another function of VGAM1885 is therefore inhibition of LOC116123 (Accession NM\_138784). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116123. LOC125929 (Accession XM\_064872) is another VGAM1885 host target gene. LOC125929 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC125929, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC125929 BINDING SITE, designated SEQ ID:37267, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62435] Another function of VGAM1885 is therefore inhibition of LOC125929 (Accession XM\_064872). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC125929. LOC142927 (Accession XM\_084380) is another VGAM1885 host target gene. LOC142927 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC142927, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142927 BINDING SITE, designated SEQ ID:37568, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62436] Another function of VGAM1885 is therefore inhibition of LOC142927 (Accession XM\_084380). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142927. LOC144893 (Accession XM\_096687) is an-

other VGAM1885 host target gene. LOC144893 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144893 BINDING SITE, designated SEQ ID:40460, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62437] Another function of VGAM1885 is therefore inhibition of LOC144893 (Accession XM\_096687). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144893. LOC145622 (Accession XM\_085186) is another VGAM1885 host target gene. LOC145622 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145622 BINDING SITE, designated SEQ ID:37904, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.



[62438] Another function of VGAM1885 is therefore inhibition of LOC145622 (Accession XM\_085186). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145622. LOC148811 (Accession XM\_086326) is another VGAM1885 host target gene. LOC148811 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148811 BINDING SITE, designated SEQ ID:38599, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62439] Another function of VGAM1885 is therefore inhibition of LOC148811 (Accession XM\_086326). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148811. LOC158156 (Accession XM\_088496) is another VGAM1885 host target gene. LOC158156 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158156, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158156 BINDING SITE, designated SEQ ID:39742, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62440] Another function of VGAM1885 is therefore inhibition of LOC158156 (Accession XM\_088496). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158156. LOC50999 (Accession NM\_016040) is another VGAM1885 host target gene. LOC50999 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC50999, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC50999 BINDING SITE, designated SEQ ID:18114, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62441] Another function of VGAM1885 is therefore inhibition of LOC50999 (Accession NM\_016040). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC50999. LOC91151 (Accession NM\_033208) is another VGAM1885 host target gene. LOC91151 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91151, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91151 BINDING SITE, designated SEQ ID:27054, to the nucleotide sequence of VGAM1885 RNA, herein designated VGAM RNA, also designated SEQ ID:4596.

[62442] Another function of VGAM1885 is therefore inhibition of LOC91151 (Accession NM\_033208). Accordingly, utilities of VGAM1885 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91151. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1886 (VGAM1886) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62443] VGAM1886 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1886 was detected is described hereinabove with reference to Figs. 1–8.

[62444] VGAM1886 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Newcastle Disease Virus. VGAM1886 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62445] VGAM1886 gene encodes a VGAM1886 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1886 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1886 precursor RNA is designated SEQ ID:1872, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1872 is located at position 7875 relative to the genome of Newcastle Disease Virus.

[62446] VGAM1886 precursor RNA folds onto itself, forming VGAM1886 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62447] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1886 folded precursor RNA into VGAM1886 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1886 RNA is designated SEQ ID:4597, and is provided hereinbelow with reference to the sequence listing part.

[62448] VGAM1886 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1886 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1886 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62449] VGAM1886 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1886 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1886 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1886 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1886 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[62450] The complementary binding of VGAM1886 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1886 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1886 host target RNA into VGAM1886 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62451] It is appreciated that VGAM1886 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1886 host target genes. The mRNA of each one of this plurality of VGAM1886 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1886 RNA, herein designated VGAM RNA, and which when bound by VGAM1886 RNA causes inhibition of translation of respective one or more VGAM1886 host target proteins.

[62452] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1886 gene, herein designated VGAM GENE, on one or more VGAM1886 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62453] It is yet further appreciated that a function of VGAM1886 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1886 include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGAM1886 correlate with, and may be deduced from, the identity of the host target genes which VGAM1886 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62454] Nucleotide sequences of the VGAM1886 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1886 RNA, herein designated VGAM RNA,



and a schematic representation of the secondary folding of VGAM1886 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1886 are further described hereinbelow with reference to Table 1.

[62455] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1886 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1886 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62456] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1886 gene, herein designated VGAM is inhibition of expression of VGAM1886 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1886 correlate with, and may be deduced from, the identity of the target genes which VGAM1886 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62457] Cadherin Related 23 (CDH23, Accession NM\_022124) is a VGAM1886 host target gene. CDH23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH23, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH23 BINDING SITE, designated SEQ ID:22668, to the nucleotide sequence of VGAM1886 RNA, herein designated VGAM RNA, also designated SEQ ID:4597.

[62458] A function of VGAM1886 is therefore inhibition of Cadherin Related 23 (CDH23, Accession NM\_022124). Accordingly, utilities of VGAM1886 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH23. TNF Receptor-associated Factor 1 (TRAF1, Accession NM\_005658) is another VGAM1886 host target gene. TRAF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAF1 BINDING SITE, designated SEQ ID:12200, to the nucleotide sequence of VGAM1886 RNA, herein designated VGAM RNA, also designated SEQ ID:4597.

[62459] Another function of VGAM1886 is therefore inhibition of TNF Receptor-associated Factor 1 (TRAF1, Accession

NM\_005658), a gene which signal transducer associated with the cytoplasmic domain of the 75 kda tumor necrosis factor receptor (tnf-r2). Accordingly, utilities of VGAM1886 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF1. The function of TRAF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM250. KIAA0893 (Accession NM\_014969) is another VGAM1886 host target gene. KIAA0893 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0893 BINDING SITE, designated SEQ ID:17360, to the nucleotide sequence of VGAM1886 RNA, herein designated VGAM RNA, also designated SEQ ID:4597.

[62460] Another function of VGAM1886 is therefore inhibition of KIAA0893 (Accession NM\_014969). Accordingly, utilities of VGAM1886 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0893. LOC203350 (Accession XM\_117536) is another

VGAM1886 host target gene. LOC203350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203350 BINDING SITE, designated SEQ ID:43531, to the nucleotide sequence of VGAM1886 RNA, herein designated VGAM RNA, also designated SEQ ID:4597.

[62461] Another function of VGAM1886 is therefore inhibition of LOC203350 (Accession XM\_117536). Accordingly, utilities of VGAM1886 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203350. LOC254413 (Accession XM\_173141) is another VGAM1886 host target gene. LOC254413 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254413 BINDING SITE, designated SEQ ID:46395, to the nucleotide sequence of VGAM1886 RNA, herein designated VGAM RNA, also designated SEQ ID:4597.

[62462] Another function of VGAM1886 is therefore inhibition of LOC254413 (Accession XM\_173141). Accordingly, utilities of VGAM1886 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254413. LOC93017 (Accession XM\_048772) is another VGAM1886 host target gene. LOC93017 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93017 BINDING SITE, designated SEQ ID:35253, to the nucleotide sequence of VGAM1886 RNA, herein designated VGAM RNA, also designated SEQ ID:4597.

[62463] Another function of VGAM1886 is therefore inhibition of LOC93017 (Accession XM\_048772). Accordingly, utilities of VGAM1886 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93017. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1887 (VGAM1887) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[62464] VGAM1887 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1887 was detected is described hereinabove with reference to Figs. 1–8.

[62465] VGAM1887 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Newcastle Disease Virus. VGAM1887 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62466] VGAM1887 gene encodes a VGAM1887 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1887 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1887 precursor RNA is designated SEQ ID:1873, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1873 is located at position 4276 relative to the genome of Newcastle Disease Virus.

[62467] VGAM1887 precursor RNA folds onto itself, forming VGAM1887 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62468] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1887 folded precursor RNA into VGAM1887 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 85%) nucleotide sequence of VGAM1887 RNA is designated SEQ ID:4598, and is provided hereinbelow with reference to the sequence listing part.

[62469] VGAM1887 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1887 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1887 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62470] VGAM1887 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1887 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1887 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1887 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1887 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in



the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62471] The complementary binding of VGAM1887 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1887 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1887 host target RNA into VGAM1887 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62472] It is appreciated that VGAM1887 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1887 host target genes. The mRNA of each one of this plurality of VGAM1887 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1887 RNA, herein designated VGAM RNA, and which when bound by VGAM1887 RNA causes inhibition of translation of respective one or more VGAM1887 host target proteins.

[62473] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1887 gene, herein designated VGAM GENE, on one or more VGAM1887 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62474] It is yet further appreciated that a function of VGAM1887 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1887 include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGAM1887 correlate with, and may be deduced from, the identity of the host target genes which VGAM1887 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[62475] Nucleotide sequences of the VGAM1887 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1887 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1887 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1887 are further described hereinbelow with reference to Table 1.

[62476] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1887 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1887 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62477] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1887 gene, herein designated VGAM is inhibition of expression of VGAM1887 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1887 correlate with, and may be deduced from, the identity of the target genes which VGAM1887 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62478] GATA Binding Protein 2 (GATA2, Accession NM\_002050) is a VGAM1887 host target gene. GATA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GATA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GATA2 BINDING SITE, designated SEQ ID:7802, to the nucleotide sequence of VGAM1887 RNA, herein designated VGAM RNA, also designated SEQ ID:4598.

[62479] A function of VGAM1887 is therefore inhibition of GATA Binding Protein 2 (GATA2, Accession NM\_002050). Accordingly, utilities of VGAM1887 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GATA2. MGC2306 (Accession NM\_032638) is another VGAM1887 host target gene. MGC2306 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2306 BINDING SITE, designated SEQ ID:26351, to the nucleotide sequence of VGAM1887 RNA,

herein designated VGAM RNA, also designated SEQ ID:4598.

[62480] Another function of VGAM1887 is therefore inhibition of MGC2306 (Accession NM\_032638). Accordingly, utilities of VGAM1887 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2306. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1888 (VGAM1888) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62481] VGAM1888 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1888 was detected is described hereinabove with reference to Figs. 1–8.

[62482] VGAM1888 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Newcastle Disease Virus. VGAM1888 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62483] VGAM1888 gene encodes a VGAM1888 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1888 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1888 precursor RNA is designated SEQ ID:1874, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1874 is located at position 12826 relative to the genome of Newcastle Disease Virus.

- [62484] VGAM1888 precursor RNA folds onto itself, forming VGAM1888 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [62485] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1888 folded precursor RNA into VGAM1888 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide sequence of VGAM1888 RNA is designated SEQ ID:4599, and is provided hereinbelow with reference to the sequence listing part.

[62486] VGAM1888 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1888 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1888 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62487] VGAM1888 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1888 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1888 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1888 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1888 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62488] The complementary binding of VGAM1888 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1888 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1888 host target RNA into VGAM1888 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62489] It is appreciated that VGAM1888 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM1888 host target genes. The mRNA of each one of this plurality of VGAM1888 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1888 RNA, herein designated VGAM RNA, and which when bound by VGAM1888 RNA causes inhibition of translation of respective one or more VGAM1888 host target proteins.

[62490] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1888 gene, herein designated VGAM GENE, on one or more VGAM1888 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[62491] It is yet further appreciated that a function of VGAM1888 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1888 include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGAM1888 correlate with, and may be deduced from, the identity of the host target genes which VGAM1888 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62492] Nucleotide sequences of the VGAM1888 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1888 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1888 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1888 are further described hereinbelow with reference to Table 1.

[62493] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1888 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1888 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62494] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1888 gene, herein designated VGAM is inhibition of expression of VGAM1888 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1888 correlate with, and may be deduced from, the identity of the target genes which VGAM1888 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62495] CD69 Antigen (p60, early T-cell activation antigen) (CD69, Accession NM\_001781) is a VGAM1888 host target gene. CD69 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD69, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD69 BINDING SITE, designated SEQ ID:7538, to the nucleotide sequence of VGAM1888 RNA, herein designated VGAM RNA, also designated SEQ ID:4599.

[62496] A function of VGAM1888 is therefore inhibition of CD69 Antigen (p60, early T-cell activation antigen) (CD69, Ac-

cession NM\_001781), a gene which is involved in lymphocyte proliferation and functions as a signal transmitting receptor. Accordingly, utilities of VGAM1888 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD69. The function of CD69 has been established by previous studies. The activation of T lymphocytes, both in vivo and in vitro, induces the expression of CD69. This molecule, which appears to be the earliest inducible cell surface glycoprotein acquired during lymphoid activation, is involved in lymphocyte proliferation and functions as a signal transmitting receptor in lymphocytes, natural killer (NK) cells, and platelets. Cambiaggi et al. (1992) produced and characterized interspecies somatic cell hybrids between human activated mature T cells and mouse BW5147 thymoma cells. A preferential segregation of human chromosomes was observed in the hybrids. They found in clones a coexpression of CD4 and CD69 antigens. Molecular and karyotypic studies of the hybrids demonstrated that the locus encoding CD69 maps to human chromosome 12 as does that for CD4 (OMIM Ref. No. 186940). Although the expression of CD69 antigen is an early event after T-lymphocyte activation and rapidly declines in the absence of exogenous

stimuli, in the hybrids they developed the expression was constitutive, similar to what is found in early thymocyte precursors and mature thymocytes. The finding suggested a dominant influence of the thymus-derived mouse tumor cell genome in controlling the constitutive expression of CD69. Lopez-Cabrera et al. (1993) demonstrated that a cDNA for CD69 showed a single open reading frame of 597 bp, predicting a 199-amino acid protein of type II membrane topology. The CD69 clone hybridized to a 1.7-kb mRNA species, which was rapidly induced and degraded after lymphocyte stimulation, consistent with the presence of rapid degradation signals at the 3-prime untranslated region. By somatic cell hybrid DNA analysis and fluorescence in situ hybridization, Lopez-Cabrera et al. (1993) assigned the CD69 gene to 12p13-p12. Protein sequence homology search demonstrated that CD69 is a member of the same superfamily of type II transmembrane receptors as natural killer cell lectin (NKG2; 161555), which also maps to chromosome 12.

[62497] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[62498] Cambiaggi, C.; Scupoli, M. T.; Cestari, T.; Gerosa, F.;

Carra, G.; Tridente, G.; Accolla, R. S. : Constitutive expression of CD69 in interspecies T-cell hybrids and locus assignment to human chromosome 12. Immunogenetics 36: 117-120, 1992. ; and

[62499] Lopez-Cabrera, M.; Santis, A. G.; Fernandez-Ruiz, E.; Blacher, R.; Esch, F.; Sanchez-Mateos, P.; Sanchez-Madrid, F. : Molecular cloning, expression, and chromosomal localization of the.

[62500] Further studies establishing the function and utilities of CD69 are found in John Hopkins OMIM database record ID 107273, and in cited publications numbered 12426-12427 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CAT56 (Accession NM\_025263) is another VGAM1888 host target gene. CAT56 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAT56, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAT56 BINDING SITE, designated SEQ ID:24931, to the nucleotide sequence of VGAM1888 RNA, herein designated VGAM RNA, also designated SEQ ID:4599.

[62501] Another function of VGAM1888 is therefore inhibition of CAT56 (Accession NM\_025263). Accordingly, utilities of VGAM1888 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAT56. FLJ20527 (Accession NM\_017863) is another VGAM1888 host target gene. FLJ20527 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20527 BINDING SITE, designated SEQ ID:19541, to the nucleotide sequence of VGAM1888 RNA, herein designated VGAM RNA, also designated SEQ ID:4599.

[62502] Another function of VGAM1888 is therefore inhibition of FLJ20527 (Accession NM\_017863). Accordingly, utilities of VGAM1888 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20527. G Protein-coupled Receptor 105 (GPR105, Accession NM\_014879) is another VGAM1888 host target gene. GPR105 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GPR105, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR105 BINDING SITE, designated SEQ ID:17021, to the nucleotide sequence of VGAM1888 RNA, herein designated VGAM RNA, also designated SEQ ID:4599.

[62503] Another function of VGAM1888 is therefore inhibition of G Protein-coupled Receptor 105 (GPR105, Accession NM\_014879). Accordingly, utilities of VGAM1888 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR105. LOC144893 (Accession XM\_096687) is another VGAM1888 host target gene. LOC144893 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144893 BINDING SITE, designated SEQ ID:40463, to the nucleotide sequence of VGAM1888 RNA, herein designated VGAM RNA, also designated SEQ ID:4599.

[62504] Another function of VGAM1888 is therefore inhibition of LOC144893 (Accession XM\_096687). Accordingly, utilities



of VGAM1888 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144893. LOC170261 (Accession XM\_093214) is another VGAM1888 host target gene. LOC170261 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC170261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170261 BINDING SITE, designated SEQ ID:40184, to the nucleotide sequence of VGAM1888 RNA, herein designated VGAM RNA, also designated SEQ ID:4599.

[62505] Another function of VGAM1888 is therefore inhibition of LOC170261 (Accession XM\_093214). Accordingly, utilities of VGAM1888 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170261. LOC257051 (Accession XM\_172800) is another VGAM1888 host target gene. LOC257051 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC257051 BINDING SITE, designated SEQ ID:46084, to the nucleotide sequence of VGAM1888 RNA, herein designated VGAM RNA, also designated SEQ ID:4599.

[62506] Another function of VGAM1888 is therefore inhibition of LOC257051 (Accession XM\_172800). Accordingly, utilities of VGAM1888 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257051. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1889 (VGAM1889) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62507] VGAM1889 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1889 was detected is described hereinabove with reference to Figs. 1–8.

[62508] VGAM1889 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Newcastle Disease Virus. VGAM1889 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62509] VGAM1889 gene encodes a VGAM1889 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1889 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1889 precursor RNA is designated SEQ ID:1875, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1875 is located at position 48 relative to the genome of Newcastle Disease Virus.

[62510] VGAM1889 precursor RNA folds onto itself, forming VGAM1889 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62511] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1889 folded precursor RNA into VGAM1889 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1889 RNA is designated SEQ ID:4600, and is provided hereinbelow with reference to the sequence listing part.

[62512] VGAM1889 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1889 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1889 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62513] VGAM1889 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1889 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1889 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1889 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1889 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62514] The complementary binding of VGAM1889 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1889 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1889 host target RNA into VGAM1889 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62515] It is appreciated that VGAM1889 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1889 host target genes. The mRNA of each one of this plurality of VGAM1889 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1889 RNA, herein designated VGAM RNA, and which when bound by VGAM1889 RNA causes inhibition of translation of respective one or more VGAM1889 host target proteins.

[62516] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1889 gene, herein designated VGAM GENE, on one or more VGAM1889 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[62517] It is yet further appreciated that a function of VGAM1889 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGAM1889 correlate with, and may be deduced from, the identity of the host target genes which VGAM1889 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62518] Nucleotide sequences of the VGAM1889 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1889 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1889 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1889 are further described hereinbelow with reference to Table 1.

[62519] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1889 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1889 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62520] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1889 gene, herein designated VGAM is inhibition of expression of VGAM1889 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1889 correlate with, and may be deduced from, the identity of the target genes which VGAM1889 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62521] Plexin A2 (PLXNA2, Accession NM\_025179) is a VGAM1889 host target gene. PLXNA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLXNA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLXNA2 BINDING SITE, designated SEQ ID:24813, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62522] A function of VGAM1889 is therefore inhibition of Plexin



A2 (PLXNA2, Accession NM\_025179), a gene which is a transmembrane protein. Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLXNA2. The function of PLXNA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM538. Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 8 (SLC7A8, Accession NM\_012244) is another VGAM1889 host target gene. SLC7A8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC7A8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A8 BINDING SITE, designated SEQ ID:14550, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62523] Another function of VGAM1889 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 8 (SLC7A8, Accession NM\_012244), a gene which helps mediate transport of large and small

neutral amino acids. Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A8. The function of SLC7A8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1263.DKFZP434F091 (Accession NM\_015453) is another VGAM1889 host target gene. DKFZP434F091 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434F091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434F091 BINDING SITE, designated SEQ ID:17736, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62524] Another function of VGAM1889 is therefore inhibition of DKFZP434F091 (Accession NM\_015453). Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434F091. FLJ13111 (Accession NM\_025082) is another VGAM1889 host target gene. FLJ13111 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13111 BINDING SITE, designated SEQ ID:24684, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62525] Another function of VGAM1889 is therefore inhibition of FLJ13111 (Accession NM\_025082). Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13111. FLJ20312 (Accession NM\_017761) is another VGAM1889 host target gene. FLJ20312 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20312 BINDING SITE, designated SEQ ID:19373, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62526] Another function of VGAM1889 is therefore inhibition of

FLJ20312 (Accession NM\_017761). Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20312. KIAA0776 (Accession XM\_035970) is another VGAM1889 host target gene. KIAA0776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0776 BINDING SITE, designated SEQ ID:32362, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62527] Another function of VGAM1889 is therefore inhibition of KIAA0776 (Accession XM\_035970). Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0776. KIAA1040 (Accession XM\_051091) is another VGAM1889 host target gene. KIAA1040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1040 BINDING SITE, designated SEQ ID:35738, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62528] Another function of VGAM1889 is therefore inhibition of KIAA1040 (Accession XM\_051091). Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1040. KIAA1956 (Accession XM\_085836) is another VGAM1889 host target gene. KIAA1956 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1956, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1956 BINDING SITE, designated SEQ ID:38361, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62529] Another function of VGAM1889 is therefore inhibition of KIAA1956 (Accession XM\_085836). Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1956. Mitogen-activated Protein Kinase Kinase Ki-

nase 2 (MAP3K2, Accession NM\_006609) is another VGAM1889 host target gene. MAP3K2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K2 BINDING SITE, designated SEQ ID:13384, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62530] Another function of VGAM1889 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 2 (MAP3K2, Accession NM\_006609). Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K2. Phospholipase A2, Group XII (PLA2G12, Accession NM\_030821) is another VGAM1889 host target gene. PLA2G12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLA2G12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2G12 BINDING SITE, designated SEQ

ID:25151, to the nucleotide sequence of VGAM1889 RNA, herein designated VGAM RNA, also designated SEQ ID:4600.

[62531] Another function of VGAM1889 is therefore inhibition of Phospholipase A2, Group XII (PLA2G12, Accession NM\_030821). Accordingly, utilities of VGAM1889 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLA2G12. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1890 (VGAM1890) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62532] VGAM1890 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1890 was detected is described hereinabove with reference to Figs. 1–8.

[62533] VGAM1890 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Newcastle Disease Virus. VGAM1890 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62534] VGAM1890 gene encodes a VGAM1890 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1890 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1890 precursor RNA is designated SEQ ID:1876, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1876 is located at position 14381 relative to the genome of Newcastle Disease Virus.

[62535] VGAM1890 precursor RNA folds onto itself, forming VGAM1890 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62536] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1890 folded precursor RNA into VGAM1890 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1890 RNA is designated SEQ ID:4601, and is provided hereinbelow with reference to the sequence listing part.

[62537] VGAM1890 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1890 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1890 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62538] VGAM1890 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1890 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1890 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1890 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1890 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62539] The complementary binding of VGAM1890 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1890 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1890 host target RNA into VGAM1890 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62540] It is appreciated that VGAM1890 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1890 host target genes. The mRNA of each one of this plurality of VGAM1890 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1890 RNA, herein designated VGAM RNA, and which when bound by VGAM1890 RNA causes inhibition of translation of respective one or more VGAM1890 host target proteins.

[62541] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1890 gene, herein designated VGAM GENE, on one or more VGAM1890 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,  
`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[62542] It is yet further appreciated that a function of VGAM1890 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1890 include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGAM1890 correlate with, and may be deduced from, the identity of the host target genes which VGAM1890 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62543] Nucleotide sequences of the VGAM1890 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1890 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1890 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1890 are further described hereinbelow with reference to Table 1.

[62544] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1890 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1890 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62545] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1890 gene, herein designated VGAM is inhibition of expression of VGAM1890 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1890 correlate with, and may be deduced from, the identity of the target genes which VGAM1890 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62546] Protein Kinase, Interferon-inducible Double Stranded RNA Dependent (PRKR, Accession NM\_002759) is a VGAM1890 host target gene. PRKR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRKR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKR BINDING SITE, designated SEQ ID:8645, to the nucleotide sequence of VGAM1890 RNA, herein designated VGAM RNA, also designated SEQ ID:4601.

[62547] A function of VGAM1890 is therefore inhibition of Protein Kinase, Interferon-inducible Double Stranded RNA Dependent (PRKR, Accession NM\_002759), a gene which catalyzes the phosphorylation of the alpha subunit of eIF2. Accordingly, utilities of VGAM1890 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKR. The function of PRKR has been established by previous studies. Ben-Asouli et al. (2002) showed that human gamma-interferon (IFNG; 147570) mRNA uses local activation of PKR in the cell to control its own translation yield. IFNG mRNA was found to activate PKR through a pseudoknot in its 5-prime untranslated region. Mutations that impaired pseudoknot stability reduced the ability to activate PKR and strongly increased the translation efficiency of IFNG mRNA. Nonphosphorylatable mutant eIF2-alpha, knockout of PKR, and the PKR inhibitors 2-aminopurine, transdominant-negative PKR, or vaccinia E3L correspondingly enhanced translation of IFNG mRNA. The potential to form the pseudoknot was found to be phylogenetically conserved. Ben-Asouli et al. (2002) proposed that the RNA pseudoknot acts to adjust translation of IFNG mRNA to the PKR level expressed in the cell. Barber et al. (1993) mapped the PRKR gene to 2p21 by in

situ hybridization. The corresponding mouse gene was mapped to chromosome 17 (band E2) by the same method. Squire et al. (1993) assigned the PRKR gene to the boundary between 2p22 and 2p21 by fluorescence in situ hybridization. Taylor et al. (1999) studied the mechanism underlying the resistance of hepatitis C virus (HCV) to interferon. They demonstrated that the HCV envelope protein E2 contains a sequence identical with phosphorylation sites of the interferon-inducible protein kinase PKR and the translation initiation factor EIF2- $\alpha$ , a target of PKR. E2 inhibited the kinase activity of PKR and blocked its inhibitory effect on protein synthesis and cell growth. This interaction of E2 in PKR may be one mechanism by which HCV circumvents the antiviral effect of interferon. Taylor et al. (1999) hypothesized that another potential outcome of PKR inhibition is the promotion of cell growth which may contribute to HCV-associated hepatocellular carcinoma. Huntington disease (OMIM Ref. No. 143100) is a neurodegenerative disorder caused by a trinucleotide repeat expansion within the huntingtin gene, resulting in generation of a polyglutamine tract in the protein product. Peel et al. (2001) showed that PKR preferentially bound mutant huntingtin RNA transcripts immobilized on strep-

tavidin columns that had been incubated with human brain extracts. Immunohistochemical studies demonstrated that PKR was present in its activated form in both human Huntington autopsy material and brain tissue derived from Huntington yeast artificial chromosome transgenic mice. The increased immunolocalization of the activated kinase was more pronounced in areas most affected by the disease. The authors suggested a role for PKR activation in the Huntington disease process.

[62548] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[62549] Ben-Asouli, Y.; Banai, Y.; Pel-Or, Y.; Shir, A.; Kaempfer, R. : Human interferon-gamma mRNA autoregulates its translation through a pseudoknot that activates the interferon-inducible protein kinase PKR. Cell 108: 221-232, 2002. ; and

[62550] Peel, A. L.; Rao, R. V.; Cottrell, B. A.; Hayden, M. R.; Ellerby, L. M.; Bredesen, D. E. : Double-stranded RNA-dependent protein kinase, PKR, binds preferentially to Huntington's diseases.

[62551] Further studies establishing the function and utilities of PRKR are found in John Hopkins OMIM database record ID



176871, and in cited publications numbered 5778, 5779–5780, 602 and 10341–10343 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ14117 (Accession NM\_022777) is another VGAM1890 host target gene. FLJ14117 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14117 BINDING SITE, designated SEQ ID:23048, to the nucleotide sequence of VGAM1890 RNA, herein designated VGAM RNA, also designated SEQ ID:4601.

[62552] Another function of VGAM1890 is therefore inhibition of FLJ14117 (Accession NM\_022777). Accordingly, utilities of VGAM1890 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14117. KIAA1464 (Accession XM\_043069) is another VGAM1890 host target gene. KIAA1464 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1464 BINDING SITE, designated SEQ ID:33880, to the nucleotide sequence of VGAM1890 RNA, herein designated VGAM RNA, also designated SEQ ID:4601.

[62553] Another function of VGAM1890 is therefore inhibition of KIAA1464 (Accession XM\_043069). Accordingly, utilities of VGAM1890 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1464. Nuclear Receptor Subfamily 1, Group I, Member 3 (NR1I3, Accession NM\_005122) is another VGAM1890 host target gene. NR1I3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NR1I3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR1I3 BINDING SITE, designated SEQ ID:11606, to the nucleotide sequence of VGAM1890 RNA, herein designated VGAM RNA, also designated SEQ ID:4601.

[62554] Another function of VGAM1890 is therefore inhibition of Nuclear Receptor Subfamily 1, Group I, Member 3 (NR1I3, Accession NM\_005122). Accordingly, utilities of VGAM1890 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with NR1I3. NY-REN-25 (Accession XM\_027116) is another VGAM1890 host target gene. NY-REN-25 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NY-REN-25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-25 BINDING SITE, designated SEQ ID:30418, to the nucleotide sequence of VGAM1890 RNA, herein designated VGAM RNA, also designated SEQ ID:4601.

[62555] Another function of VGAM1890 is therefore inhibition of NY-REN-25 (Accession XM\_027116). Accordingly, utilities of VGAM1890 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-25. LOC199858 (Accession XM\_114040) is another VGAM1890 host target gene. LOC199858 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199858 BINDING SITE, designated SEQ ID:42632, to

the nucleotide sequence of VGAM1890 RNA, herein designated VGAM RNA, also designated SEQ ID:4601.

[62556] Another function of VGAM1890 is therefore inhibition of LOC199858 (Accession XM\_114040). Accordingly, utilities of VGAM1890 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199858. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1891 (VGAM1891) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62557] VGAM1891 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1891 was detected is described hereinabove with reference to Figs. 1–8.

[62558] VGAM1891 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Newcastle Disease Virus. VGAM1891 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62559] VGAM1891 gene encodes a VGAM1891 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1891 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1891 precursor RNA is designated SEQ ID:1877, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1877 is located at position 8373 relative to the genome of Newcastle Disease Virus.

[62560] VGAM1891 precursor RNA folds onto itself, forming VGAM1891 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62561] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1891 folded precursor RNA into VGAM1891 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM1891 RNA is designated SEQ ID:4602, and is provided hereinbelow with reference to the sequence listing part.

[62562] VGAM1891 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1891 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1891 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62563] VGAM1891 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1891 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1891 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1891 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1891 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62564] The complementary binding of VGAM1891 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1891 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1891 host target RNA into VGAM1891 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62565] It is appreciated that VGAM1891 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1891 host target genes. The mRNA of each one of this plurality of VGAM1891 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1891 RNA, herein designated VGAM RNA, and which when bound by VGAM1891 RNA causes inhibition of translation of respective one or more VGAM1891 host target proteins.

[62566] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1891 gene, herein designated VGAM GENE, on one or more VGAM1891 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[62567] It is yet further appreciated that a function of VGAM1891 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGAM1891 correlate with, and may be deduced from, the identity of the host target genes which VGAM1891 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62568] Nucleotide sequences of the VGAM1891 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1891 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1891 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1891 are further described hereinbelow with reference to Table 1.

[62569] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1891 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1891 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62570] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1891 gene, herein designated VGAM is inhibition of expression of VGAM1891 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1891 correlate with, and may be deduced from, the identity of the target genes which VGAM1891 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62571] ATP10C (Accession NM\_024490) is a VGAM1891 host target gene. ATP10C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP10C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP10C BINDING SITE, designated SEQ ID:23686, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62572] A function of VGAM1891 is therefore inhibition of ATP10C (Accession NM\_024490), a gene which is phosphorylated

in their intermediate state, drives uphill transport of ions across membranes. Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP10C. The function of ATP10C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM801. Collagen, Type XIII, Alpha 1 (COL13A1, Accession NM\_080799) is another VGAM1891 host target gene. COL13A1 BINDING SITE1 through COL13A1 BINDING SITE7 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL13A1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL13A1 BINDING SITE1 through COL13A1 BINDING SITE7, designated SEQ ID:28065, SEQ ID:28067, SEQ ID:28069, SEQ ID:28071, SEQ ID:28073, SEQ ID:28075 and SEQ ID:11702 respectively, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62573] Another function of VGAM1891 is therefore inhibition of Collagen, Type XIII, Alpha 1 (COL13A1, Accession

NM\_080799), a gene which is specific for basement membranes. Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL13A1. The function of COL13A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1680. KIAA0157 (Accession NM\_032182) is another VGAM1891 host target gene. KIAA0157 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0157 BINDING SITE, designated SEQ ID:25896, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62574] Another function of VGAM1891 is therefore inhibition of KIAA0157 (Accession NM\_032182). Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0157. KIAA1193 (Accession XM\_041843) is another VGAM1891 host target gene. KIAA1193 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1193 BINDING SITE, designated SEQ ID:33584, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62575] Another function of VGAM1891 is therefore inhibition of KIAA1193 (Accession XM\_041843). Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1193. MGC3248 (Accession NM\_032486) is another VGAM1891 host target gene. MGC3248 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3248 BINDING SITE, designated SEQ ID:26235, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62576] Another function of VGAM1891 is therefore inhibition of

MGC3248 (Accession NM\_032486). Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3248. PGCP (Accession NM\_016134) is another VGAM1891 host target gene. PGCP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PGCP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PGCP BINDING SITE, designated SEQ ID:18220, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62577] Another function of VGAM1891 is therefore inhibition of PGCP (Accession NM\_016134). Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PGCP. PRO0529 (Accession NM\_014074) is another VGAM1891 host target gene. PRO0529 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PRO0529 BINDING SITE, designated SEQ ID:15297, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62578] Another function of VGAM1891 is therefore inhibition of PRO0529 (Accession NM\_014074). Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0529. LOC149706 (Accession XM\_097718) is another VGAM1891 host target gene. LOC149706 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149706 BINDING SITE, designated SEQ ID:41057, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62579] Another function of VGAM1891 is therefore inhibition of LOC149706 (Accession XM\_097718). Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149706. LOC152373 (Accession XM\_087449) is an-

other VGAM1891 host target gene. LOC152373 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152373 BINDING SITE, designated SEQ ID:39271, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62580] Another function of VGAM1891 is therefore inhibition of LOC152373 (Accession XM\_087449). Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152373. LOC221477 (Accession XM\_166397) is another VGAM1891 host target gene. LOC221477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221477 BINDING SITE, designated SEQ ID:44256, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.



[62581] Another function of VGAM1891 is therefore inhibition of LOC221477 (Accession XM\_166397). Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221477. LOC90167 (Accession XM\_029570) is another VGAM1891 host target gene. LOC90167 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90167, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90167 BINDING SITE, designated SEQ ID:30905, to the nucleotide sequence of VGAM1891 RNA, herein designated VGAM RNA, also designated SEQ ID:4602.

[62582] Another function of VGAM1891 is therefore inhibition of LOC90167 (Accession XM\_029570). Accordingly, utilities of VGAM1891 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90167. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1892 (VGAM1892) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[62583] VGAM1892 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1892 was detected is described hereinabove with reference to Figs. 1-8.

[62584] VGAM1892 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Newcastle Disease Virus. VGAM1892 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62585] VGAM1892 gene encodes a VGAM1892 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1892 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1892 precursor RNA is designated SEQ ID:1878, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1878 is located at position 13642 relative to the genome of Newcastle Disease Virus.

[62586] VGAM1892 precursor RNA folds onto itself, forming VGAM1892 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62587] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1892 folded precursor RNA into VGAM1892 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1892 RNA is designated SEQ ID:4603, and is provided hereinbelow with reference to the sequence listing part.

[62588] VGAM1892 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1892 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1892 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62589] VGAM1892 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1892 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1892 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1892 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1892 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62590] The complementary binding of VGAM1892 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1892 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1892 host target RNA into VGAM1892 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62591] It is appreciated that VGAM1892 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1892 host target genes. The mRNA of each one of this plurality of VGAM1892 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1892 RNA, herein designated VGAM RNA, and which when bound by VGAM1892 RNA causes inhibition of translation of respective one or more VGAM1892 host target proteins.

[62592] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1892 gene, herein designated VGAM GENE, on one or more VGAM1892 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62593] It is yet further appreciated that a function of VGAM1892 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGAM1892 correlate with, and may be deduced from, the identity of the host target genes which VGAM1892 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[62594] Nucleotide sequences of the VGAM1892 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1892 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1892 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1892 are further described hereinbelow with reference to Table 1.

[62595] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1892 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1892 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62596] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1892 gene, herein designated VGAM is inhibition of expression of VGAM1892 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1892 correlate with, and may be deduced from, the identity of the target genes which VGAM1892 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62597] Apoptotic Protease Activating Factor (APAF1, Accession NM\_001160) is a VGAM1892 host target gene. APAF1 BINDING SITE1 and APAF1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by APAF1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APAF1 BINDING SITE1 and APAF1 BINDING SITE2, designated SEQ ID:6828 and SEQ ID:14867 respectively, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62598] A function of VGAM1892 is therefore inhibition of Apoptotic Protease Activating Factor (APAF1, Accession NM\_001160), a gene which functions in the mitochondrial apoptotic pathway that leads to caspase 9 dependent activation of caspase 3. Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APAF1. The function of APAF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552.Aquaporin 6, Kidney Specific (AQP6, Accession



NM\_053286) is another VGAM1892 host target gene.

AQP6 BINDING SITE1 and AQP6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AQP6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP6 BINDING SITE1 and AQP6 BINDING SITE2, designated SEQ ID:27620 and SEQ ID:14511 respectively, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62599] Another function of VGAM1892 is therefore inhibition of Aquaporin 6, Kidney Specific (AQP6, Accession NM\_053286), a gene which participates in distinct physiologic function such as glomerular filtration, tubular endocytosis, and acid-base metabolism. Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AQP6. The function of AQP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340.SORCS1 (Accession NM\_052918) is another VGAM1892 host target gene. SORCS1 BINDING SITE

is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SORCS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORCS1 BINDING SITE, designated SEQ ID:27486, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62600] Another function of VGAM1892 is therefore inhibition of SORCS1 (Accession NM\_052918). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORCS1. Zic Family Member 3 Heterotaxy 1 (odd-paired homolog, Drosophila) (ZIC3, Accession NM\_003413) is another VGAM1892 host target gene. ZIC3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZIC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZIC3 BINDING SITE, designated SEQ ID:9451, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62601] Another function of VGAM1892 is therefore inhibition of Zic Family Member 3 Heterotaxy 1 (odd-paired homolog, *Drosophila*) (ZIC3, Accession NM\_003413). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZIC3. D21S2056E (Accession NM\_003683) is another VGAM1892 host target gene. D21S2056E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by D21S2056E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D21S2056E BINDING SITE, designated SEQ ID:9789, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62602] Another function of VGAM1892 is therefore inhibition of D21S2056E (Accession NM\_003683). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D21S2056E. FLJ12154 (Accession NM\_021944) is another VGAM1892 host target gene. FLJ12154 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12154, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12154 BINDING SITE, designated SEQ ID:22463, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62603] Another function of VGAM1892 is therefore inhibition of FLJ12154 (Accession NM\_021944). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12154. Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654) is another VGAM1892 host target gene. SDC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC3 BINDING SITE, designated SEQ ID:16089, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62604] Another function of VGAM1892 is therefore inhibition of Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654). Accordingly, utilities of VGAM1892 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with SDC3. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4C (SEMA4C, Accession NM\_017789) is another VGAM1892 host target gene. SEMA4C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA4C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4C BINDING SITE, designated SEQ ID:19420, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62605] Another function of VGAM1892 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4C (SEMA4C, Accession NM\_017789). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4C. LOC130074 (Accession XM\_072228) is another VGAM1892 host target gene. LOC130074 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by LOC130074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130074 BINDING SITE, designated SEQ ID:37469, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62606] Another function of VGAM1892 is therefore inhibition of LOC130074 (Accession XM\_072228). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130074. LOC144681 (Accession XM\_096654) is another VGAM1892 host target gene. LOC144681 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144681 BINDING SITE, designated SEQ ID:40453, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62607] Another function of VGAM1892 is therefore inhibition of

LOC144681 (Accession XM\_096654). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144681. LOC148438 (Accession XM\_097466) is another VGAM1892 host target gene. LOC148438 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148438 BINDING SITE, designated SEQ ID:40883, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62608] Another function of VGAM1892 is therefore inhibition of LOC148438 (Accession XM\_097466). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148438. LOC203276 (Accession XM\_117523) is another VGAM1892 host target gene. LOC203276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC203276 BINDING SITE, designated SEQ ID:43490, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62609] Another function of VGAM1892 is therefore inhibition of LOC203276 (Accession XM\_117523). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203276. LOC203305 (Accession XM\_117529) is another VGAM1892 host target gene. LOC203305 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203305 BINDING SITE, designated SEQ ID:43514, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62610] Another function of VGAM1892 is therefore inhibition of LOC203305 (Accession XM\_117529). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203305. LOC254243 (Accession XM\_173233) is an-



other VGAM1892 host target gene. LOC254243 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254243 BINDING SITE, designated SEQ ID:46516, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62611] Another function of VGAM1892 is therefore inhibition of LOC254243 (Accession XM\_173233). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254243. LOC254887 (Accession XM\_172326) is another VGAM1892 host target gene. LOC254887 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254887, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254887 BINDING SITE, designated SEQ ID:46071, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62612] Another function of VGAM1892 is therefore inhibition of LOC254887 (Accession XM\_172326). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254887. LOC90038 (Accession XM\_028305) is another VGAM1892 host target gene. LOC90038 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90038 BINDING SITE, designated SEQ ID:30653, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62613] Another function of VGAM1892 is therefore inhibition of LOC90038 (Accession XM\_028305). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90038. LOC92078 (Accession XM\_042684) is another VGAM1892 host target gene. LOC92078 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC92078, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92078 BINDING SITE, designated SEQ ID:33741, to the nucleotide sequence of VGAM1892 RNA, herein designated VGAM RNA, also designated SEQ ID:4603.

[62614] Another function of VGAM1892 is therefore inhibition of LOC92078 (Accession XM\_042684). Accordingly, utilities of VGAM1892 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92078. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1893 (VGAM1893) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62615] VGAM1893 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1893 was detected is described hereinabove with reference to Figs. 1-8.

[62616] VGAM1893 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Newcastle Disease Virus. VGAM1893 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[62617] VGAM1893 gene encodes a VGAM1893 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1893 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1893 precursor RNA is designated SEQ ID:1879, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1879 is located at position 2483 relative to the genome of Newcastle Disease Virus.

[62618] VGAM1893 precursor RNA folds onto itself, forming VGAM1893 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62619] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1893 folded precursor RNA into VGAM1893

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1893 RNA is designated SEQ ID:4604, and is provided hereinbelow with reference to the sequence listing part.

[62620] VGAM1893 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1893 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1893 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62621] VGAM1893 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1893 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1893 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1893 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1893 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62622] The complementary binding of VGAM1893 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1893 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1893 host target RNA into VGAM1893 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[62623] It is appreciated that VGAM1893 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1893 host target genes. The mRNA of each one of this plurality of VGAM1893 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1893 RNA, herein designated VGAM RNA, and which when bound by VGAM1893 RNA causes inhibition of translation of respective one or more VGAM1893 host target proteins.

[62624] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1893 gene, herein designated VGAM GENE, on one or more VGAM1893 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62625] It is yet further appreciated that a function of VGAM1893 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGAM1893 correlate with, and may be deduced from, the identity of the host target genes which VGAM1893 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62626] Nucleotide sequences of the VGAM1893 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1893 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1893 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1893 are further described hereinbelow with reference to Table 1.

[62627] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1893 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1893 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62628] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1893 gene, herein designated VGAM is inhibition of expression of VGAM1893 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1893 correlate with, and may be deduced from, the identity of the target genes which VGAM1893 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62629] S-adenosylmethionine Decarboxylase 1 (AMD1, Accession NM\_001634) is a VGAM1893 host target gene. AMD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMD1 BINDING SITE, designated SEQ ID:7349, to the nucleotide sequence of VGAM1893 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4604.

[62630] A function of VGAM1893 is therefore inhibition of S-adenosylmethionine Decarboxylase 1 (AMD1, Accession NM\_001634), a gene which catalyzes the removal of the carboxylate group of S-adenosylmethionine in the polyamine biosynthesis pathway. Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMD1. The function of AMD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1016. Collagen, Type IV, Alpha 6 (COL4A6, Accession NM\_033641) is another VGAM1893 host target gene. COL4A6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by COL4A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A6 BINDING SITE, designated SEQ ID:27359, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62631] Another function of VGAM1893 is therefore inhibition of

Collagen, Type IV, Alpha 6 (COL4A6, Accession NM\_033641). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A6. Coronin, Actin Binding Protein, 2B (CORO2B, Accession XM\_035403) is another VGAM1893 host target gene. CORO2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CORO2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CORO2B BINDING SITE, designated SEQ ID:32254, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62632] Another function of VGAM1893 is therefore inhibition of Coronin, Actin Binding Protein, 2B (CORO2B, Accession XM\_035403), a gene which may play a role in the reorganization of neuronal actin structure. Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CORO2B. The function of CORO2B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM923.FAT Tumor Suppressor Homolog 2 (Drosophila) (FAT2, Accession NM\_001447) is another VGAM1893 host target gene. FAT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FAT2 BINDING SITE, designated SEQ ID:7175, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62633] Another function of VGAM1893 is therefore inhibition of FAT Tumor Suppressor Homolog 2 (Drosophila) (FAT2, Accession NM\_001447), a gene which could function as a cell-adhesion protein. Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAT2. The function of FAT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM949.Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM\_002531) is another VGAM1893 host target gene. NTSR1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by NTSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTSR1 BINDING SITE, designated SEQ ID:8366, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62634] Another function of VGAM1893 is therefore inhibition of Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM\_002531), a gene which is associated with g proteins that activate a phosphatidylinositol– calcium second messenger system. Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTSR1. The function of NTSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Procollagen–proline, 2–oxoglutarate 4–dioxygenase (proline 4–hydroxylase), Beta Polypeptide (protein disulfide isomerase; thyroid hormone binding protein p55) (P4HB, Accession NM\_000918) is another VGAM1893 host target gene. P4HB BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by P4HB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P4HB BINDING SITE, designated SEQ ID:6630, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62635] Another function of VGAM1893 is therefore inhibition of Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), Beta Polypeptide (protein disulfide isomerase; thyroid hormone binding protein p55) (P4HB, Accession NM\_000918), a gene which catalyzes formation of 4-hydroxyproline in collagens. Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P4HB. The function of P4HB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM589. Pim-2 Oncogene (PIM2, Accession XM\_010208) is another VGAM1893 host target gene. PIM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIM2, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIM2 BINDING SITE, designated SEQ ID:30134, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62636] Another function of VGAM1893 is therefore inhibition of Pim-2 Oncogene (PIM2, Accession XM\_010208). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIM2. Short Stature Homeobox (SHOX, Accession NM\_000451) is another VGAM1893 host target gene. SHOX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SHOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHOX BINDING SITE, designated SEQ ID:6059, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62637] Another function of VGAM1893 is therefore inhibition of Short Stature Homeobox (SHOX, Accession NM\_000451). Accordingly, utilities of VGAM1893 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with SHOX. Chromosome 20 Open Reading Frame 39 (C20orf39, Accession NM\_024893) is another VGAM1893 host target gene. C20orf39 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf39 BINDING SITE, designated SEQ ID:24368, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62638] Another function of VGAM1893 is therefore inhibition of Chromosome 20 Open Reading Frame 39 (C20orf39, Accession NM\_024893). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf39. Chromosome 20 Open Reading Frame 45 (C20orf45, Accession NM\_016045) is another VGAM1893 host target gene. C20orf45 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf45, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.



Table 2 illustrates the complementarity of the nucleotide sequences of C20orf45 BINDING SITE, designated SEQ ID:18122, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62639] Another function of VGAM1893 is therefore inhibition of Chromosome 20 Open Reading Frame 45 (C20orf45, Accession NM\_016045). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf45. CLONE24945 (Accession NM\_015683) is another VGAM1893 host target gene. CLONE24945 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLONE24945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLONE24945 BINDING SITE, designated SEQ ID:17907, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62640] Another function of VGAM1893 is therefore inhibition of CLONE24945 (Accession NM\_015683). Accordingly, utilities of VGAM1893 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with CLONE24945. FLJ11320 (Accession NM\_018389) is another VGAM1893 host target gene. FLJ11320 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11320 BINDING SITE, designated SEQ ID:20429, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62641] Another function of VGAM1893 is therefore inhibition of FLJ11320 (Accession NM\_018389). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11320. FLJ23112 (Accession NM\_024929) is another VGAM1893 host target gene. FLJ23112 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23112 BINDING SITE, designated SEQ ID:24466, to the nucleotide

sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62642] Another function of VGAM1893 is therefore inhibition of FLJ23112 (Accession NM\_024929). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23112. G Protein-coupled Receptor Kinase-interactor 1 (GIT1, Accession NM\_014030) is another VGAM1893 host target gene. GIT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GIT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT1 BINDING SITE, designated SEQ ID:15259, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62643] Another function of VGAM1893 is therefore inhibition of G Protein-coupled Receptor Kinase-interactor 1 (GIT1, Accession NM\_014030). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT1. KIAA1203 (Accession XM\_049683) is another VGAM1893 host target

gene. KIAA1203 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1203, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1203 BINDING SITE, designated SEQ ID:35473, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62644] Another function of VGAM1893 is therefore inhibition of KIAA1203 (Accession XM\_049683). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1203. KIAA1538 (Accession XM\_049474) is another VGAM1893 host target gene. KIAA1538 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1538 BINDING SITE, designated SEQ ID:35434, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62645] Another function of VGAM1893 is therefore inhibition of KIAA1538 (Accession XM\_049474). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1538. KIAA1655 (Accession XM\_039442) is another VGAM1893 host target gene. KIAA1655 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1655 BINDING SITE, designated SEQ ID:33088, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62646] Another function of VGAM1893 is therefore inhibition of KIAA1655 (Accession XM\_039442). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1655. KIAA1937 (Accession XM\_057107) is another VGAM1893 host target gene. KIAA1937 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1937, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1937 BINDING SITE, designated SEQ ID:36483, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62647] Another function of VGAM1893 is therefore inhibition of KIAA1937 (Accession XM\_057107). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1937. NDRG Family Member 4 (NDRG4, Accession NM\_020465) is another VGAM1893 host target gene. NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NDRG4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2, designated SEQ ID:21698 and SEQ ID:23213 respectively, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62648] Another function of VGAM1893 is therefore inhibition of NDRG Family Member 4 (NDRG4, Accession NM\_020465).

Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG4. Ubiquitin-like, Containing PHD and RING Finger Domains, 1 (UHRF1, Accession NM\_013282) is another VGAM1893 host target gene. UHRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UHRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UHRF1 BINDING SITE, designated SEQ ID:14954, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62649] Another function of VGAM1893 is therefore inhibition of Ubiquitin-like, Containing PHD and RING Finger Domains, 1 (UHRF1, Accession NM\_013282). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UHRF1. YME1-like 1 (*S. cerevisiae*) (YME1L1, Accession NM\_014263) is another VGAM1893 host target gene. YME1L1 BINDING SITE1 and YME1L1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions

of mRNA encoded by YME1L1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YME1L1 BINDING SITE1 and YME1L1 BINDING SITE2, designated SEQ ID:15539 and SEQ ID:29295 respectively, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62650] Another function of VGAM1893 is therefore inhibition of YME1-like 1 (*S. cerevisiae*) (YME1L1, Accession NM\_014263). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YME1L1. LOC165405 (Accession XM\_092567) is another VGAM1893 host target gene. LOC165405 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC165405, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165405 BINDING SITE, designated SEQ ID:40130, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.



[62651] Another function of VGAM1893 is therefore inhibition of LOC165405 (Accession XM\_092567). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165405. LOC202908 (Accession XM\_114602) is another VGAM1893 host target gene. LOC202908 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202908 BINDING SITE, designated SEQ ID:42997, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62652] Another function of VGAM1893 is therefore inhibition of LOC202908 (Accession XM\_114602). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202908. LOC91149 (Accession XM\_036480) is another VGAM1893 host target gene. LOC91149 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91149, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91149 BINDING SITE, designated SEQ ID:32457, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62653] Another function of VGAM1893 is therefore inhibition of LOC91149 (Accession XM\_036480). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91149. LOC93276 (Accession XM\_050200) is another VGAM1893 host target gene. LOC93276 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93276 BINDING SITE, designated SEQ ID:35590, to the nucleotide sequence of VGAM1893 RNA, herein designated VGAM RNA, also designated SEQ ID:4604.

[62654] Another function of VGAM1893 is therefore inhibition of LOC93276 (Accession XM\_050200). Accordingly, utilities of VGAM1893 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC93276. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1894 (VGAM1894) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62655] VGAM1894 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1894 was detected is described hereinabove with reference to Figs. 1–8.

[62656] VGAM1894 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Respiratory Syncytial Virus. VGAM1894 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62657] VGAM1894 gene encodes a VGAM1894 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1894 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1894 precursor RNA is designated SEQ ID:1880, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1880 is located at position 6434 relative to the genome of Respiratory Syncytial Virus.

- [62658] VGAM1894 precursor RNA folds onto itself, forming VGAM1894 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [62659] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1894 folded precursor RNA into VGAM1894 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1894 RNA is designated SEQ ID:4605, and is provided hereinbelow with reference to the sequence listing part.

[62660] VGAM1894 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1894 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1894 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62661] VGAM1894 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1894 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1894 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1894 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1894 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[62662] The complementary binding of VGAM1894 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1894 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1894 host target RNA into VGAM1894 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62663] It is appreciated that VGAM1894 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1894 host target genes. The mRNA of each one of this plurality of VGAM1894 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1894 RNA, herein designated VGAM RNA, and which when bound by VGAM1894 RNA causes

inhibition of translation of respective one or more VGAM1894 host target proteins.

[62664] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1894 gene, herein designated VGAM GENE, on one or more VGAM1894 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62665] It is yet further appreciated that a function of VGAM1894 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1894 include diagnosis, prevention and

treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1894 correlate with, and may be deduced from, the identity of the host target genes which VGAM1894 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62666] Nucleotide sequences of the VGAM1894 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1894 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1894 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1894 are further described hereinbelow with reference to Table 1.

[62667] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1894 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1894 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62668] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1894 gene, herein designated VGAM is inhibition of expression of VGAM1894 target genes. It is



appreciated that specific functions, and accordingly utilities, of VGAM1894 correlate with, and may be deduced from, the identity of the target genes which VGAM1894 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62669] Lanosterol Synthase (2,3-oxidosqualene-lanosterol cyclase) (LSS, Accession NM\_002340) is a VGAM1894 host target gene. LSS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LSS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LSS BINDING SITE, designated SEQ ID:8140, to the nucleotide sequence of VGAM1894 RNA, herein designated VGAM RNA, also designated SEQ ID:4605.

[62670] A function of VGAM1894 is therefore inhibition of Lanosterol Synthase (2,3-oxidosqualene-lanosterol cyclase) (LSS, Accession NM\_002340). Accordingly, utilities of VGAM1894 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LSS. Chondrolectin (CHODL, Accession NM\_024944) is another VGAM1894 host target gene. CHODL BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by CHODL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHODL BINDING SITE, designated SEQ ID:24492, to the nucleotide sequence of VGAM1894 RNA, herein designated VGAM RNA, also designated SEQ ID:4605.

[62671] Another function of VGAM1894 is therefore inhibition of Chondrolectin (CHODL, Accession NM\_024944). Accordingly, utilities of VGAM1894 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHODL. FLJ12057 (Accession NM\_024768) is another VGAM1894 host target gene. FLJ12057 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12057 BINDING SITE, designated SEQ ID:24124, to the nucleotide sequence of VGAM1894 RNA, herein designated VGAM RNA, also designated SEQ ID:4605.

[62672] Another function of VGAM1894 is therefore inhibition of FLJ12057 (Accession NM\_024768). Accordingly, utilities of

VGAM1894 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12057. FLJ23360 (Accession NM\_023076) is another VGAM1894 host target gene. FLJ23360 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23360, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23360 BINDING SITE, designated SEQ ID:23337, to the nucleotide sequence of VGAM1894 RNA, herein designated VGAM RNA, also designated SEQ ID:4605.

[62673] Another function of VGAM1894 is therefore inhibition of FLJ23360 (Accession NM\_023076). Accordingly, utilities of VGAM1894 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23360. Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM\_145255) is another VGAM1894 host target gene. MRPL10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of MRPL10 BINDING SITE, designated SEQ ID:29771, to the nucleotide sequence of VGAM1894 RNA, herein designated VGAM RNA, also designated SEQ ID:4605.

[62674] Another function of VGAM1894 is therefore inhibition of Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM\_145255). Accordingly, utilities of VGAM1894 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL10. LOC143680 (Accession XM\_096474) is another VGAM1894 host target gene. LOC143680 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143680, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143680 BINDING SITE, designated SEQ ID:40375, to the nucleotide sequence of VGAM1894 RNA, herein designated VGAM RNA, also designated SEQ ID:4605.

[62675] Another function of VGAM1894 is therefore inhibition of LOC143680 (Accession XM\_096474). Accordingly, utilities of VGAM1894 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC143680. LOC256433 (Accession XM\_173657) is another VGAM1894 host target gene. LOC256433 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256433, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256433 BINDING SITE, designated SEQ ID:46553, to the nucleotide sequence of VGAM1894 RNA, herein designated VGAM RNA, also designated SEQ ID:4605.

[62676] Another function of VGAM1894 is therefore inhibition of LOC256433 (Accession XM\_173657). Accordingly, utilities of VGAM1894 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256433. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1895 (VGAM1895) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62677] VGAM1895 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1895 was detected is described hereinabove with reference to Figs. 1–8.

[62678] VGAM1895 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Latent Virus.

VGAM1895 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62679] VGAM1895 gene encodes a VGAM1895 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1895 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1895 precursor RNA is designated SEQ ID:1881, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1881 is located at position 2156 relative to the genome of Garlic Latent Virus.

[62680] VGAM1895 precursor RNA folds onto itself, forming VGAM1895 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62681] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1895 folded precursor RNA into VGAM1895 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1895 RNA is designated SEQ ID:4606, and is provided hereinbelow with reference to the sequence listing part.

[62682] VGAM1895 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1895 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1895 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62683] VGAM1895 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1895 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1895 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1895 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1895 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[62684] The complementary binding of VGAM1895 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM1895 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1895 host target RNA into VGAM1895 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62685] It is appreciated that VGAM1895 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1895 host target genes. The mRNA of each one of this plurality of VGAM1895 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1895 RNA, herein designated VGAM RNA, and which when bound by VGAM1895 RNA causes inhibition of translation of respective one or more VGAM1895 host target proteins.

[62686] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1895 gene, herein designated VGAM GENE, on one or more VGAM1895 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62687] It is yet further appreciated that a function of VGAM1895 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1895 include diagnosis, prevention and treatment of viral infection by Garlic Latent Virus. Specific functions, and accordingly utilities, of VGAM1895 correlate with, and may be deduced from, the identity of the host target genes which VGAM1895 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62688] Nucleotide sequences of the VGAM1895 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1895 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1895 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1895 are further described hereinbelow with reference to Table 1.

[62689] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1895 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1895 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62690] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1895 gene, herein designated VGAM is inhibition of expression of VGAM1895 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1895 correlate with, and may be deduced from, the identity of the target genes which VGAM1895 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62691] DKFZP434E2135 (Accession NM\_030804) is a VGAM1895 host target gene. DKFZP434E2135 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434E2135, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434E2135 BINDING SITE, designated SEQ ID:25118, to the nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62692] A function of VGAM1895 is therefore inhibition of DKFZP434E2135 (Accession NM\_030804). Accordingly, utilities of VGAM1895 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434E2135. KIAA0563 (Accession NM\_014834) is another VGAM1895 host target gene. KIAA0563 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0563 BINDING SITE, designated SEQ ID:16846, to the nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62693] Another function of VGAM1895 is therefore inhibition of KIAA0563 (Accession NM\_014834). Accordingly, utilities of VGAM1895 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0563. KIAA1503 (Accession XM\_043197) is another VGAM1895 host target gene. KIAA1503 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1503, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1503 BINDING SITE, designated SEQ ID:33918, to the nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62694] Another function of VGAM1895 is therefore inhibition of KIAA1503 (Accession XM\_043197). Accordingly, utilities of VGAM1895 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1503. KIAA1958 (Accession XM\_088566) is another VGAM1895 host target gene. KIAA1958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1958 BINDING SITE, designated SEQ ID:39832, to the

nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62695] Another function of VGAM1895 is therefore inhibition of KIAA1958 (Accession XM\_088566). Accordingly, utilities of VGAM1895 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1958. LOC112609 (Accession XM\_053013) is another VGAM1895 host target gene. LOC112609 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112609 BINDING SITE, designated SEQ ID:36057, to the nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62696] Another function of VGAM1895 is therefore inhibition of LOC112609 (Accession XM\_053013). Accordingly, utilities of VGAM1895 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112609. LOC147071 (Accession XM\_054031) is another VGAM1895 host target gene. LOC147071 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC147071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147071 BINDING SITE, designated SEQ ID:36140, to the nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62697] Another function of VGAM1895 is therefore inhibition of LOC147071 (Accession XM\_054031). Accordingly, utilities of VGAM1895 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147071. LOC149271 (Accession XM\_086475) is another VGAM1895 host target gene. LOC149271 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149271 BINDING SITE, designated SEQ ID:38677, to the nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62698] Another function of VGAM1895 is therefore inhibition of LOC149271 (Accession XM\_086475). Accordingly, utilities

of VGAM1895 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149271. LOC221092 (Accession XM\_167749) is another VGAM1895 host target gene. LOC221092 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221092 BINDING SITE, designated SEQ ID:44775, to the nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62699] Another function of VGAM1895 is therefore inhibition of LOC221092 (Accession XM\_167749). Accordingly, utilities of VGAM1895 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221092. LOC255328 (Accession XM\_172920) is another VGAM1895 host target gene. LOC255328 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255328, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences



of LOC255328 BINDING SITE, designated SEQ ID:46180, to the nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62700] Another function of VGAM1895 is therefore inhibition of LOC255328 (Accession XM\_172920). Accordingly, utilities of VGAM1895 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255328. LOC92719 (Accession XM\_046853) is another VGAM1895 host target gene. LOC92719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92719 BINDING SITE, designated SEQ ID:34849, to the nucleotide sequence of VGAM1895 RNA, herein designated VGAM RNA, also designated SEQ ID:4606.

[62701] Another function of VGAM1895 is therefore inhibition of LOC92719 (Accession XM\_046853). Accordingly, utilities of VGAM1895 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92719. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1896 (VGAM1896) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62702] VGAM1896 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1896 was detected is described hereinabove with reference to Figs. 1–8.

[62703] VGAM1896 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Respiratory Syncytial Virus. VGAM1896 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62704] VGAM1896 gene encodes a VGAM1896 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1896 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1896 precursor RNA is designated SEQ ID:1882, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1882 is located at position 4399 relative to the

genome of Respiratory Syncytial Virus.

[62705] VGAM1896 precursor RNA folds onto itself, forming VGAM1896 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62706] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1896 folded precursor RNA into VGAM1896 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1896 RNA is designated SEQ ID:4607, and is provided hereinbelow with reference to the sequence listing part.

[62707] VGAM1896 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1896 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1896 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[62708] VGAM1896 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1896 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1896 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1896 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1896 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62709] The complementary binding of VGAM1896 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1896 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1896 host target RNA into VGAM1896 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62710] It is appreciated that VGAM1896 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1896 host target genes. The mRNA of each one of this plurality of VGAM1896 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1896 RNA, herein designated VGAM RNA, and which when bound by VGAM1896 RNA causes inhibition of translation of respective one or more VGAM1896 host target proteins.

[62711] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1896 gene, herein designated VGAM GENE, on one or more VGAM1896 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62712] It is yet further appreciated that a function of VGAM1896 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1896 include diagnosis, prevention and treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1896

correlate with, and may be deduced from, the identity of the host target genes which VGAM1896 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62713] Nucleotide sequences of the VGAM1896 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1896 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1896 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1896 are further described hereinbelow with reference to Table 1.

[62714] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1896 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1896 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62715] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1896 gene, herein designated VGAM is inhibition of expression of VGAM1896 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1896 correlate with, and may be deduced

from, the identity of the target genes which VGAM1896 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62716] Protein Phosphatase 1, Catalytic Subunit, Beta Isoform (PPP1CB, Accession NM\_002709) is a VGAM1896 host target gene. PPP1CB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1CB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1CB BINDING SITE, designated SEQ ID:8558, to the nucleotide sequence of VGAM1896 RNA, herein designated VGAM RNA, also designated SEQ ID:4607.

[62717] A function of VGAM1896 is therefore inhibition of Protein Phosphatase 1, Catalytic Subunit, Beta Isoform (PPP1CB, Accession NM\_002709), a gene which is the catalytic subunit of protein phosphatase 1. Accordingly, utilities of VGAM1896 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1CB. The function of PPP1CB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with



reference to VGAM46.BY55 (Accession XM\_001667) is another VGAM1896 host target gene. BY55 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BY55, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BY55 BINDING SITE, designated SEQ ID:29845, to the nucleotide sequence of VGAM1896 RNA, herein designated VGAM RNA, also designated SEQ ID:4607.

[62718] Another function of VGAM1896 is therefore inhibition of BY55 (Accession XM\_001667). Accordingly, utilities of VGAM1896 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BY55. KIAA1042 (Accession NM\_014965) is another VGAM1896 host target gene. KIAA1042 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1042 BINDING SITE, designated SEQ ID:17353, to the nucleotide sequence of VGAM1896 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4607.

[62719] Another function of VGAM1896 is therefore inhibition of KIAA1042 (Accession NM\_014965). Accordingly, utilities of VGAM1896 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1042. MAWBP (Accession NM\_022129) is another VGAM1896 host target gene. MAWBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAWBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAWBP BINDING SITE, designated SEQ ID:22681, to the nucleotide sequence of VGAM1896 RNA, herein designated VGAM RNA, also designated SEQ ID:4607.

[62720] Another function of VGAM1896 is therefore inhibition of MAWBP (Accession NM\_022129). Accordingly, utilities of VGAM1896 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAWBP. MEGF10 (Accession NM\_032446) is another VGAM1896 host target gene. MEGF10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEGF10, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEGF10 BINDING SITE, designated SEQ ID:26209, to the nucleotide sequence of VGAM1896 RNA, herein designated VGAM RNA, also designated SEQ ID:4607.

[62721] Another function of VGAM1896 is therefore inhibition of MEGF10 (Accession NM\_032446). Accordingly, utilities of VGAM1896 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEGF10. LOC151361 (Accession XM\_098048) is another VGAM1896 host target gene. LOC151361 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151361 BINDING SITE, designated SEQ ID:41333, to the nucleotide sequence of VGAM1896 RNA, herein designated VGAM RNA, also designated SEQ ID:4607.

[62722] Another function of VGAM1896 is therefore inhibition of LOC151361 (Accession XM\_098048). Accordingly, utilities of VGAM1896 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC151361. LOC162333 (Accession XM\_102591) is another VGAM1896 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42130, to the nucleotide sequence of VGAM1896 RNA, herein designated VGAM RNA, also designated SEQ ID:4607.

[62723] Another function of VGAM1896 is therefore inhibition of LOC162333 (Accession XM\_102591). Accordingly, utilities of VGAM1896 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC201725 (Accession XM\_114370) is another VGAM1896 host target gene. LOC201725 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC201725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201725 BINDING SITE, designated SEQ ID:42905, to

the nucleotide sequence of VGAM1896 RNA, herein designated VGAM RNA, also designated SEQ ID:4607.

[62724] Another function of VGAM1896 is therefore inhibition of LOC201725 (Accession XM\_114370). Accordingly, utilities of VGAM1896 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201725. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1897 (VGAM1897) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62725] VGAM1897 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1897 was detected is described hereinabove with reference to Figs. 1–8.

[62726] VGAM1897 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Latent Virus. VGAM1897 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62727] VGAM1897 gene encodes a VGAM1897 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1897 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1897 precursor RNA is designated SEQ ID:1883, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1883 is located at position 5382 relative to the genome of Garlic Latent Virus.

[62728] VGAM1897 precursor RNA folds onto itself, forming VGAM1897 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62729] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1897 folded precursor RNA into VGAM1897 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1897 RNA is designated SEQ ID:4608, and is provided hereinbelow with reference to the sequence listing part.

[62730] VGAM1897 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1897 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1897 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62731] VGAM1897 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1897 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1897 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1897 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1897 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62732] The complementary binding of VGAM1897 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1897 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1897 host target RNA into VGAM1897 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62733] It is appreciated that VGAM1897 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM1897 host target genes. The mRNA of each one of this plurality of VGAM1897 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1897 RNA, herein designated VGAM RNA, and which when bound by VGAM1897 RNA causes inhibition of translation of respective one or more VGAM1897 host target proteins.

[62734] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1897 gene, herein designated VGAM GENE, on one or more VGAM1897 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[62735] It is yet further appreciated that a function of VGAM1897 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of viral infection by Garlic Latent Virus. Specific functions, and accordingly utilities, of VGAM1897 correlate with, and may be deduced from, the identity of the host target genes which VGAM1897 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62736] Nucleotide sequences of the VGAM1897 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1897 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1897 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1897 are further described hereinbelow with reference to Table 1.

[62737] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1897 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1897 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62738] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1897 gene, herein designated VGAM is inhibition of expression of VGAM1897 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1897 correlate with, and may be deduced from, the identity of the target genes which VGAM1897 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62739] Microfibrillar-associated Protein 3 (MFAP3, Accession NM\_005927) is a VGAM1897 host target gene. MFAP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MFAP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MFAP3 BINDING SITE, designated SEQ ID:12555, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62740] A function of VGAM1897 is therefore inhibition of Microfibrillar-associated Protein 3 (MFAP3, Accession

NM\_005927). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MFAP3. Pro-melanin-concentrating Hormone-like 1 (PMCHL1, Accession NM\_031887) is another VGAM1897 host target gene. PMCHL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMCHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMCHL1 BINDING SITE, designated SEQ ID:25631, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62741] Another function of VGAM1897 is therefore inhibition of Pro-melanin-concentrating Hormone-like 1 (PMCHL1, Accession NM\_031887). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMCHL1. Calcium Binding Atopy-related Autoantigen 1 (CBARA1, Accession NM\_006077) is another VGAM1897 host target gene. CBARA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

CBARA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBARA1 BINDING SITE, designated SEQ ID:12723, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62742] Another function of VGAM1897 is therefore inhibition of Calcium Binding Atopy-related Autoantigen 1 (CBARA1, Accession NM\_006077). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBARA1. FLJ10704 (Accession NM\_018185) is another VGAM1897 host target gene. FLJ10704 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10704 BINDING SITE, designated SEQ ID:20033, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62743] Another function of VGAM1897 is therefore inhibition of

FLJ10704 (Accession NM\_018185). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10704. FLJ13456 (Accession XM\_038291) is another VGAM1897 host target gene. FLJ13456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13456 BINDING SITE, designated SEQ ID:32798, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62744] Another function of VGAM1897 is therefore inhibition of FLJ13456 (Accession XM\_038291). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13456. KIAA1013 (Accession XM\_114303) is another VGAM1897 host target gene. KIAA1013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1013 BINDING SITE, designated SEQ ID:42857, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62745] Another function of VGAM1897 is therefore inhibition of KIAA1013 (Accession XM\_114303). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1013. MGC32104 (Accession NM\_144684) is another VGAM1897 host target gene. MGC32104 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC32104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC32104 BINDING SITE, designated SEQ ID:29505, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62746] Another function of VGAM1897 is therefore inhibition of MGC32104 (Accession NM\_144684). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC32104. Serine Palmitoyltransferase, Long Chain Base

Subunit 2 (SPTLC2, Accession NM\_004863) is another VGAM1897 host target gene. SPTLC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTLC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTLC2 BINDING SITE, designated SEQ ID:11277, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62747] Another function of VGAM1897 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM\_004863). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. Upstream Binding Protein 1 (LBP-1a) (UBP1, Accession NM\_014517) is another VGAM1897 host target gene. UBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBP1 BINDING SITE, designated SEQ ID:15846,



to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62748] Another function of VGAM1897 is therefore inhibition of Upstream Binding Protein 1 (LBP-1a) (UBP1, Accession NM\_014517). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBP1. LOC144348 (Accession XM\_084826) is another VGAM1897 host target gene. LOC144348 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144348, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144348 BINDING SITE, designated SEQ ID:37721, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62749] Another function of VGAM1897 is therefore inhibition of LOC144348 (Accession XM\_084826). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144348. LOC196418 (Accession XM\_113717) is another VGAM1897 host target gene. LOC196418 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196418 BINDING SITE, designated SEQ ID:42369, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62750] Another function of VGAM1897 is therefore inhibition of LOC196418 (Accession XM\_113717). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196418. LOC221362 (Accession XM\_168093) is another VGAM1897 host target gene. LOC221362 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221362 BINDING SITE, designated SEQ ID:45020, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62751] Another function of VGAM1897 is therefore inhibition of

LOC221362 (Accession XM\_168093). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221362. LOC254672 (Accession XM\_170619) is another VGAM1897 host target gene. LOC254672 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254672, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254672 BINDING SITE, designated SEQ ID:45398, to the nucleotide sequence of VGAM1897 RNA, herein designated VGAM RNA, also designated SEQ ID:4608.

[62752] Another function of VGAM1897 is therefore inhibition of LOC254672 (Accession XM\_170619). Accordingly, utilities of VGAM1897 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254672. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1898 (VGAM1898) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[62753] VGAM1898 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1898 was detected is described hereinabove with reference to Figs. 1–8.

[62754] VGAM1898 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Latent Virus. VGAM1898 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62755] VGAM1898 gene encodes a VGAM1898 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1898 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1898 precursor RNA is designated SEQ ID:1884, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1884 is located at position 4971 relative to the genome of Garlic Latent Virus.

[62756] VGAM1898 precursor RNA folds onto itself, forming VGAM1898 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62757] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1898 folded precursor RNA into VGAM1898 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1898 RNA is designated SEQ ID:4609, and is provided hereinbelow with reference to the sequence listing part.

[62758] VGAM1898 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1898 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1898 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[62759] VGAM1898 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1898 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1898 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1898 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1898 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[62760] The complementary binding of VGAM1898 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1898 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1898 host target RNA into VGAM1898 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62761] It is appreciated that VGAM1898 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1898 host target genes. The mRNA of each one of this plurality of VGAM1898 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1898 RNA, herein designated VGAM RNA, and which when bound by VGAM1898 RNA causes inhibition of translation of respective one or more VGAM1898 host target proteins.

[62762] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1898 gene, herein designated VGAM GENE, on one

or more VGAM1898 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62763] It is yet further appreciated that a function of VGAM1898 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1898 include diagnosis, prevention and treatment of viral infection by Garlic Latent Virus. Specific functions, and accordingly utilities, of VGAM1898 correlate with, and may be deduced from, the identity of the host target genes which VGAM1898 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[62764] Nucleotide sequences of the VGAM1898 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1898 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1898 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1898 are further described hereinbelow with reference to Table 1.

[62765] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1898 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1898 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62766] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1898 gene, herein designated VGAM is inhibition of expression of VGAM1898 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1898 correlate with, and may be deduced from, the identity of the target genes which VGAM1898 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62767] Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Acces-

sion NM\_053023) is a VGAM1898 host target gene. ZFP91 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP91, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP91 BINDING SITE, designated SEQ ID:27571, to the nucleotide sequence of VGAM1898 RNA, herein designated VGAM RNA, also designated SEQ ID:4609.

[62768] A function of VGAM1898 is therefore inhibition of Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM\_053023). Accordingly, utilities of VGAM1898 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP91. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1899 (VGAM1899) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62769] VGAM1899 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1899 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[62770] VGAM1899 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Respiratory Syncytial Virus. VGAM1899 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62771] VGAM1899 gene encodes a VGAM1899 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1899 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1899 precursor RNA is designated SEQ ID:1885, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1885 is located at position 7191 relative to the genome of Respiratory Syncytial Virus.

[62772] VGAM1899 precursor RNA folds onto itself, forming VGAM1899 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62773] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1899 folded precursor RNA into VGAM1899 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1899 RNA is designated SEQ ID:4610, and is provided hereinbelow with reference to the sequence listing part.

[62774] VGAM1899 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1899 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1899 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62775] VGAM1899 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1899 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1899 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1899 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1899 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62776] The complementary binding of VGAM1899 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1899 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1899 host target RNA into VGAM1899 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62777] It is appreciated that VGAM1899 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1899 host target genes. The mRNA of each one of this plurality of VGAM1899 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1899 RNA, herein designated VGAM RNA, and which when bound by VGAM1899 RNA causes inhibition of translation of respective one or more VGAM1899 host target proteins.

[62778] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1899 gene, herein designated VGAM GENE, on one or more VGAM1899 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62779] It is yet further appreciated that a function of VGAM1899 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1899 correlate with, and may be deduced from, the identity of the host target genes which VGAM1899 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62780] Nucleotide sequences of the VGAM1899 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1899 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1899 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1899 are further described hereinbelow with reference to Table 1.

[62781] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1899 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1899 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62782] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1899 gene, herein designated VGAM is inhibition of expression of VGAM1899 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1899 correlate with, and may be deduced from, the identity of the target genes which VGAM1899 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62783] Fibrillin 1 (Marfan syndrome) (FBN1, Accession XM\_034890) is a VGAM1899 host target gene. FBN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBN1, corresponding to a HOST TARGET binding site such as BINDING SITE



I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBN1 BINDING SITE, designated SEQ ID:32183, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62784] A function of VGAM1899 is therefore inhibition of Fibrillin 1 (Marfan syndrome) (FBN1, Accession XM\_034890). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBN1. GNAS Complex Locus (GNAS, Accession NM\_016592) is another VGAM1899 host target gene. GNAS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAS BINDING SITE, designated SEQ ID:18678, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62785] Another function of VGAM1899 is therefore inhibition of GNAS Complex Locus (GNAS, Accession NM\_016592), a gene which transduces signals from G protein-coupled receptors and activates adenylyl cyclase. Accordingly, util-

ities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAS. The function of GNAS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1205. Tropomodulin (TMOD, Accession NM\_003275) is another VGAM1899 host target gene. TMOD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TMOD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMOD BINDING SITE, designated SEQ ID:9295, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62786] Another function of VGAM1899 is therefore inhibition of Tropomodulin (TMOD, Accession NM\_003275), a gene which blocks the elongation and depolymerization of the actin filaments at the pointed end. Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMOD. The function of TMOD and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM716.ATP-binding Cassette, Sub-family A (ABC1), Member 8 (ABCA8, Accession NM\_007168) is another VGAM1899 host target gene. ABCA8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ABCA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCA8 BINDING SITE, designated SEQ ID:14013, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62787] Another function of VGAM1899 is therefore inhibition of ATP-binding Cassette, Sub-family A (ABC1), Member 8 (ABCA8, Accession NM\_007168). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCA8. Baculoviral IAP Repeat-containing 1 (BIRC1, Accession NM\_004536) is another VGAM1899 host target gene. BIRC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BIRC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of BIRC1 BINDING SITE, designated SEQ ID:10884, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62788] Another function of VGAM1899 is therefore inhibition of Baculoviral IAP Repeat-containing 1 (BIRC1, Accession NM\_004536). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC1. FLJ10508 (Accession NM\_018118) is another VGAM1899 host target gene. FLJ10508 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10508 BINDING SITE, designated SEQ ID:19893, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62789] Another function of VGAM1899 is therefore inhibition of FLJ10508 (Accession NM\_018118). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10508. FLJ12747 (Accession NM\_032173) is another VGAM1899 host target gene. FLJ12747 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12747, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12747 BINDING SITE, designated SEQ ID:25878, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62790] Another function of VGAM1899 is therefore inhibition of FLJ12747 (Accession NM\_032173). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12747. KIAA0527 (Accession XM\_171054) is another VGAM1899 host target gene. KIAA0527 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0527 BINDING SITE, designated SEQ ID:45850, to the nucleotide sequence of VGAM1899 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4610.

[62791] Another function of VGAM1899 is therefore inhibition of KIAA0527 (Accession XM\_171054). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0527. KIAA1948 (Accession XM\_091984) is another VGAM1899 host target gene. KIAA1948 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1948, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1948 BINDING SITE, designated SEQ ID:40077, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62792] Another function of VGAM1899 is therefore inhibition of KIAA1948 (Accession XM\_091984). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1948. NESHBP (Accession NM\_015429) is another VGAM1899 host target gene. NESHBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NESHBP, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NESHBP BINDING SITE, designated SEQ ID:17728, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62793] Another function of VGAM1899 is therefore inhibition of NESHBP (Accession NM\_015429). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NESHBP. P311 (Accession NM\_004772) is another VGAM1899 host target gene. P311 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P311, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P311 BINDING SITE, designated SEQ ID:11161, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62794] Another function of VGAM1899 is therefore inhibition of P311 (Accession NM\_004772). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with P311. Pleckstrin Homology Domain Interacting Protein (PHIP, Accession NM\_017934) is another VGAM1899 host target gene. PHIP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PHIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHIP BINDING SITE, designated SEQ ID:19622, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62795] Another function of VGAM1899 is therefore inhibition of Pleckstrin Homology Domain Interacting Protein (PHIP, Accession NM\_017934). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHIP. Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM\_004863) is another VGAM1899 host target gene. SPTLC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTLC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide



sequences of SPTLC2 BINDING SITE, designated SEQ ID:11273, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62796] Another function of VGAM1899 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM\_004863). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. LOC144747 (Accession XM\_084954) is another VGAM1899 host target gene. LOC144747 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144747, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144747 BINDING SITE, designated SEQ ID:37783, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62797] Another function of VGAM1899 is therefore inhibition of LOC144747 (Accession XM\_084954). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC144747. LOC149372 (Accession XM\_086509) is another VGAM1899 host target gene. LOC149372 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149372, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149372 BINDING SITE, designated SEQ ID:38723, to the nucleotide sequence of VGAM1899 RNA, herein designated VGAM RNA, also designated SEQ ID:4610.

[62798] Another function of VGAM1899 is therefore inhibition of LOC149372 (Accession XM\_086509). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149372. LOC257463 (Accession XM\_048605) is another VGAM1899 host target gene. LOC257463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257463 BINDING SITE, designated SEQ ID:35206, to the nucleotide sequence of VGAM1899 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4610.

[62799] Another function of VGAM1899 is therefore inhibition of LOC257463 (Accession XM\_048605). Accordingly, utilities of VGAM1899 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257463. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1900 (VGAM1900) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62800] VGAM1900 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1900 was detected is described hereinabove with reference to Figs. 1–8.

[62801] VGAM1900 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Respiratory Syncytial Virus. VGAM1900 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62802] VGAM1900 gene encodes a VGAM1900 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1900 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1900 precursor RNA is designated SEQ ID:1886, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1886 is located at position 438 relative to the genome of Respiratory Syncytial Virus.

[62803] VGAM1900 precursor RNA folds onto itself, forming VGAM1900 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62804] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1900 folded precursor RNA into VGAM1900 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM1900 RNA is designated SEQ ID:4611, and is provided hereinbelow with reference to the sequence listing part.

[62805] VGAM1900 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1900 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1900 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62806] VGAM1900 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1900 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1900 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1900 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1900 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62807] The complementary binding of VGAM1900 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1900 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1900 host target RNA into VGAM1900 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62808] It is appreciated that VGAM1900 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1900 host target genes. The mRNA of

each one of this plurality of VGAM1900 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1900 RNA, herein designated VGAM RNA, and which when bound by VGAM1900 RNA causes inhibition of translation of respective one or more VGAM1900 host target proteins.

[62809] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1900 gene, herein designated VGAM GENE, on one or more VGAM1900 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[62810] It is yet further appreciated that a function of VGAM1900 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1900 correlate with, and may be deduced from, the identity of the host target genes which VGAM1900 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62811] Nucleotide sequences of the VGAM1900 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1900 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1900 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1900 are further described hereinbelow with reference to Table 1.

[62812] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1900 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1900 RNA,



herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62813] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1900 gene, herein designated VGAM is inhibition of expression of VGAM1900 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1900 correlate with, and may be deduced from, the identity of the target genes which VGAM1900 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62814] Adenylate Cyclase 2 (brain) (ADCY2, Accession XM\_036383) is a VGAM1900 host target gene. ADCY2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADCY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY2 BINDING SITE, designated SEQ ID:32435, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62815] A function of VGAM1900 is therefore inhibition of Adenylate Cyclase 2 (brain) (ADCY2, Accession XM\_036383), a gene which Adenylate cyclase (type 2), an ATP-

pyrophosphate lyase; converts ATP to cAMP. Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY2. The function of ADCY2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. EGF-like-domain, Multiple 5 (EGFL5, Accession XM\_098838) is another VGAM1900 host target gene. EGFL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL5 BINDING SITE, designated SEQ ID:41886, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62816] Another function of VGAM1900 is therefore inhibition of EGF-like-domain, Multiple 5 (EGFL5, Accession XM\_098838). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL5. Interferon, Gamma-inducible Protein 16 (IFI16, Accession XM\_048826) is an-

other VGAM1900 host target gene. IFI16 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by IFI16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IFI16 BINDING SITE, designated SEQ ID:35282, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62817] Another function of VGAM1900 is therefore inhibition of Interferon, Gamma-inducible Protein 16 (IFI16, Accession XM\_048826), a gene which could have a role in the regulation of hematopoietic differentiation and controls cellular proliferation. Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IFI16. The function of IFI16 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1182. Chromosome 12 Open Reading Frame 22 (C12orf22, Accession NM\_030809) is another VGAM1900 host target gene. C12orf22 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by C12orf22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C12orf22 BINDING SITE, designated SEQ ID:25124, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62818] Another function of VGAM1900 is therefore inhibition of Chromosome 12 Open Reading Frame 22 (C12orf22, Accession NM\_030809). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C12orf22. Calcyphosphine 2 (CAPS2, Accession XM\_047354) is another VGAM1900 host target gene. CAPS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPS2 BINDING SITE, designated SEQ ID:34953, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62819] Another function of VGAM1900 is therefore inhibition of

Calcyphosphine 2 (CAPS2, Accession XM\_047354). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPS2. CTP Synthase II (CTPS2, Accession NM\_019857) is another VGAM1900 host target gene. CTPS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTPS2 BINDING SITE, designated SEQ ID:21264, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62820] Another function of VGAM1900 is therefore inhibition of CTP Synthase II (CTPS2, Accession NM\_019857). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTPS2. FLJ10300 (Accession NM\_018051) is another VGAM1900 host target gene. FLJ10300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10300, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10300 BINDING SITE, designated SEQ ID:19811, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62821] Another function of VGAM1900 is therefore inhibition of FLJ10300 (Accession NM\_018051). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10300. SCYA28 (Accession NM\_019846) is another VGAM1900 host target gene. SCYA28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCYA28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYA28 BINDING SITE, designated SEQ ID:21251, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62822] Another function of VGAM1900 is therefore inhibition of SCYA28 (Accession NM\_019846). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

SCYA28. STHM (Accession NM\_006456) is another VGAM1900 host target gene. STHM BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STHM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STHM BINDING SITE, designated SEQ ID:13177, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62823] Another function of VGAM1900 is therefore inhibition of STHM (Accession NM\_006456). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STHM. LOC151429 (Accession XM\_098059) is another VGAM1900 host target gene. LOC151429 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151429 BINDING SITE, designated SEQ ID:41344, to the nucleotide sequence of VGAM1900 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4611.

[62824] Another function of VGAM1900 is therefore inhibition of LOC151429 (Accession XM\_098059). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151429. LOC153454 (Accession XM\_087672) is another VGAM1900 host target gene. LOC153454 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153454, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153454 BINDING SITE, designated SEQ ID:39376, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62825] Another function of VGAM1900 is therefore inhibition of LOC153454 (Accession XM\_087672). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153454. LOC203504 (Accession XM\_117550) is another VGAM1900 host target gene. LOC203504 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203504, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203504 BINDING SITE, designated SEQ ID:43573, to the nucleotide sequence of VGAM1900 RNA, herein designated VGAM RNA, also designated SEQ ID:4611.

[62826] Another function of VGAM1900 is therefore inhibition of LOC203504 (Accession XM\_117550). Accordingly, utilities of VGAM1900 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203504. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1901 (VGAM1901) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62827] VGAM1901 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1901 was detected is described hereinabove with reference to Figs. 1-8.

[62828] VGAM1901 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Respiratory Syncytial

Virus. VGAM1901 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62829] VGAM1901 gene encodes a VGAM1901 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1901 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1901 precursor RNA is designated SEQ ID:1887, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1887 is located at position 2370 relative to the genome of Respiratory Syncytial Virus.

[62830] VGAM1901 precursor RNA folds onto itself, forming VGAM1901 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62831] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1901 folded precursor RNA into VGAM1901 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM1901 RNA is designated SEQ ID:4612, and is provided hereinbelow with reference to the sequence listing part.

[62832] VGAM1901 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1901 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1901 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62833] VGAM1901 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1901 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1901 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1901 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1901 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62834] The complementary binding of VGAM1901 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1901 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1901 host target RNA into VGAM1901 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62835] It is appreciated that VGAM1901 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1901 host target genes. The mRNA of each one of this plurality of VGAM1901 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1901 RNA, herein designated VGAM RNA, and which when bound by VGAM1901 RNA causes inhibition of translation of respective one or more VGAM1901 host target proteins.

[62836] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1901 gene, herein designated VGAM GENE, on one or more VGAM1901 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62837] It is yet further appreciated that a function of VGAM1901 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1901 include diagnosis, prevention and treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1901 correlate with, and may be deduced from, the identity of the host target genes which VGAM1901 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62838] Nucleotide sequences of the VGAM1901 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1901 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1901 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1901 are further described hereinbelow with reference to Table 1.

[62839] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1901 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1901 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62840] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1901 gene, herein designated VGAM is inhibition of expression of VGAM1901 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1901 correlate with, and may be deduced from, the identity of the target genes which VGAM1901 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62841] C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252) is a VGAM1901 host target gene. CLECSF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLECSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of CLECSF5 BINDING SITE, designated SEQ ID:14915, to the nucleotide sequence of VGAM1901 RNA, herein designated VGAM RNA, also designated SEQ ID:4612.

[62842] A function of VGAM1901 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252). Accordingly, utilities of VGAM1901 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF5. Estrogen-related Receptor Gamma (ESRRG, Accession XM\_039053) is another VGAM1901 host target gene. ESRRG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESRRG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESRRG BINDING SITE, designated SEQ ID:32993, to the nucleotide sequence of VGAM1901 RNA, herein designated VGAM RNA, also designated SEQ ID:4612.

[62843] Another function of VGAM1901 is therefore inhibition of Estrogen-related Receptor Gamma (ESRRG, Accession XM\_039053), a gene which Estrogen-related receptor



gamma. Accordingly, utilities of VGAM1901 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESRRG. The function of ESRRG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM359.F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM\_033644) is another VGAM1901 host target gene. FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FBXW1B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3, designated SEQ ID:27362, SEQ ID:27372 and SEQ ID:14660 respectively, to the nucleotide sequence of VGAM1901 RNA, herein designated VGAM RNA, also designated SEQ ID:4612.

[62844] Another function of VGAM1901 is therefore inhibition of F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM\_033644), a gene which somehow is involved in the process of neuronal cell differentiation or brain develop-

ment. Accordingly, utilities of VGAM1901 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXW1B. The function of FBXW1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25.SMA3 (Accession NM\_006780) is another VGAM1901 host target gene. SMA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMA3 BINDING SITE, designated SEQ ID:13653, to the nucleotide sequence of VGAM1901 RNA, herein designated VGAM RNA, also designated SEQ ID:4612.

[62845] Another function of VGAM1901 is therefore inhibition of SMA3 (Accession NM\_006780). Accordingly, utilities of VGAM1901 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMA3. LOC151056 (Accession XM\_087088) is another VGAM1901 host target gene. LOC151056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151056, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151056 BINDING SITE, designated SEQ ID:39046, to the nucleotide sequence of VGAM1901 RNA, herein designated VGAM RNA, also designated SEQ ID:4612.

[62846] Another function of VGAM1901 is therefore inhibition of LOC151056 (Accession XM\_087088). Accordingly, utilities of VGAM1901 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151056. LOC157247 (Accession XM\_088275) is another VGAM1901 host target gene. LOC157247 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157247 BINDING SITE, designated SEQ ID:39572, to the nucleotide sequence of VGAM1901 RNA, herein designated VGAM RNA, also designated SEQ ID:4612.

[62847] Another function of VGAM1901 is therefore inhibition of LOC157247 (Accession XM\_088275). Accordingly, utilities of VGAM1901 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC157247. LOC222066 (Accession XM\_166582) is another VGAM1901 host target gene. LOC222066 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222066, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222066 BINDING SITE, designated SEQ ID:44553, to the nucleotide sequence of VGAM1901 RNA, herein designated VGAM RNA, also designated SEQ ID:4612.

[62848] Another function of VGAM1901 is therefore inhibition of LOC222066 (Accession XM\_166582). Accordingly, utilities of VGAM1901 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222066. LOC254504 (Accession XM\_173192) is another VGAM1901 host target gene. LOC254504 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254504 BINDING SITE, designated SEQ ID:46437, to

the nucleotide sequence of VGAM1901 RNA, herein designated VGAM RNA, also designated SEQ ID:4612.

[62849] Another function of VGAM1901 is therefore inhibition of LOC254504 (Accession XM\_173192). Accordingly, utilities of VGAM1901 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254504. LOC90520 (Accession XM\_032277) is another VGAM1901 host target gene. LOC90520 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90520 BINDING SITE, designated SEQ ID:31629, to the nucleotide sequence of VGAM1901 RNA, herein designated VGAM RNA, also designated SEQ ID:4612.

[62850] Another function of VGAM1901 is therefore inhibition of LOC90520 (Accession XM\_032277). Accordingly, utilities of VGAM1901 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90520. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1902 (VGAM1902) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62851] VGAM1902 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1902 was detected is described hereinabove with reference to Figs. 1–8.

[62852] VGAM1902 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Respiratory Syncytial Virus. VGAM1902 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62853] VGAM1902 gene encodes a VGAM1902 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1902 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1902 precursor RNA is designated SEQ ID:1888, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1888 is located at position 8673 relative to the genome of Respiratory Syncytial Virus.

[62854] VGAM1902 precursor RNA folds onto itself, forming VGAM1902 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62855] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1902 folded precursor RNA into VGAM1902 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1902 RNA is designated SEQ ID:4613, and is provided hereinbelow with reference to the sequence listing part.

[62856] VGAM1902 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1902 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1902 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[62857] VGAM1902 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1902 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1902 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1902 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1902 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding



sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62858] The complementary binding of VGAM1902 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1902 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1902 host target RNA into VGAM1902 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62859] It is appreciated that VGAM1902 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1902 host target genes. The mRNA of each one of this plurality of VGAM1902 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1902 RNA, herein designated VGAM RNA, and which when bound by VGAM1902 RNA causes inhibition of translation of respective one or more VGAM1902 host target proteins.

[62860] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1902 gene, herein designated VGAM GENE, on one or more VGAM1902 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62861] It is yet further appreciated that a function of VGAM1902 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1902 include diagnosis, prevention and treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1902 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1902 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62862] Nucleotide sequences of the VGAM1902 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1902 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1902 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1902 are further described hereinbelow with reference to Table 1.

[62863] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1902 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1902 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62864] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1902 gene, herein designated VGAM is inhibition of expression of VGAM1902 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1902 correlate with, and may be deduced from, the identity of the target genes which VGAM1902

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62865] PRO2015 (Accession NM\_018512) is a VGAM1902 host target gene. PRO2015 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO2015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2015 BINDING SITE, designated SEQ ID:20585, to the nucleotide sequence of VGAM1902 RNA, herein designated VGAM RNA, also designated SEQ ID:4613.

[62866] A function of VGAM1902 is therefore inhibition of PRO2015 (Accession NM\_018512). Accordingly, utilities of VGAM1902 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2015. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1903 (VGAM1903) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62867] VGAM1903 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1903 was detected is described hereinabove with reference to Figs. 1–8.

[62868] VGAM1903 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Respiratory Syncytial Virus. VGAM1903 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62869] VGAM1903 gene encodes a VGAM1903 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1903 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1903 precursor RNA is designated SEQ ID:1889, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1889 is located at position 14231 relative to the genome of Respiratory Syncytial Virus.

[62870] VGAM1903 precursor RNA folds onto itself, forming VGAM1903 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62871] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1903 folded precursor RNA into VGAM1903 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1903 RNA is designated SEQ ID:4614, and is provided hereinbelow with reference to the sequence listing part.

[62872] VGAM1903 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1903 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1903 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[62873] VGAM1903 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1903 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1903 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1903 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1903 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62874] The complementary binding of VGAM1903 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1903 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1903 host target RNA into VGAM1903 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62875] It is appreciated that VGAM1903 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1903 host target genes. The mRNA of each one of this plurality of VGAM1903 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1903 RNA, herein designated VGAM RNA, and which when bound by VGAM1903 RNA causes inhibition of translation of respective one or more VGAM1903 host target proteins.

[62876] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1903 gene, herein designated VGAM GENE, on one or more VGAM1903 host target gene, herein designated



VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62877] It is yet further appreciated that a function of VGAM1903 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1903 correlate with, and may be deduced from, the identity of the host target genes which VGAM1903 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62878] Nucleotide sequences of the VGAM1903 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1903 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1903 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1903 are further  
described hereinbelow with reference to Table 1.

[62879] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1903 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1903 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[62880] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1903 gene, herein designated VGAM is  
inhibition of expression of VGAM1903 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1903 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1903  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[62881] Mucin 3B (MUC3B, Accession XM\_168578) is a VGAM1903  
host target gene. MUC3B BINDING SITE is HOST TARGET

binding site found in the 5' untranslated region of mRNA encoded by MUC3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC3B BINDING SITE, designated SEQ ID:45254, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62882] A function of VGAM1903 is therefore inhibition of Mucin 3B (MUC3B, Accession XM\_168578), a gene which provides a protective, lubricating barrier against particles and infectious agents at mucosal surfaces. Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC3B. The function of MUC3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Reelin (RELN, Accession XM\_168628) is another VGAM1903 host target gene. RELN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RELN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of RELN BINDING SITE, designated SEQ ID:45282, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62883] Another function of VGAM1903 is therefore inhibition of Reelin (RELN, Accession XM\_168628), a gene which regulates microtubule function in neurons and neuronal migration. Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RELN. The function of RELN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM35. Selectin L (lymphocyte adhesion molecule 1) (SELL, Accession NM\_000655) is another VGAM1903 host target gene. SELL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SELL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SELL BINDING SITE, designated SEQ ID:6315, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62884] Another function of VGAM1903 is therefore inhibition of Selectin L (lymphocyte adhesion molecule 1) (SELL, Accession NM\_000655), a gene which is a cell surface adhesion protein. Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SELL. The function of SELL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM374. WW Domain Containing Oxidoreductase (WWOX, Accession NM\_016373) is another VGAM1903 host target gene. WWOX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WWOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WWOX BINDING SITE, designated SEQ ID:18505, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62885] Another function of VGAM1903 is therefore inhibition of WW Domain Containing Oxidoreductase (WWOX, Accession NM\_016373), a gene which involves in protein-

protein interactions and may contribute to the biologic consequences of DNA instability. Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WWOX. The function of WWOX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM644.DKFZP434C131 (Accession XM\_044630) is another VGAM1903 host target gene. DKFZP434C131 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434C131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C131 BINDING SITE, designated SEQ ID:34242, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62886] Another function of VGAM1903 is therefore inhibition of DKFZP434C131 (Accession XM\_044630). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C131. DKFZP564K0322 (Accession

NM\_032040) is another VGAM1903 host target gene. DKFZP564K0322 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP564K0322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564K0322 BINDING SITE, designated SEQ ID:25739, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62887] Another function of VGAM1903 is therefore inhibition of DKFZP564K0322 (Accession NM\_032040). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564K0322. F-box Only Protein 21 (FBXO21, Accession NM\_033624) is another VGAM1903 host target gene. FBXO21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO21 BINDING SITE, designated SEQ ID:27322, to the nucleotide sequence of VGAM1903 RNA,

herein designated VGAM RNA, also designated SEQ ID:4614.

[62888] Another function of VGAM1903 is therefore inhibition of F-box Only Protein 21 (FBXO21, Accession NM\_033624). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO21. FLJ30927 (Accession NM\_144690) is another VGAM1903 host target gene. FLJ30927 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ30927, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30927 BINDING SITE, designated SEQ ID:29509, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62889] Another function of VGAM1903 is therefore inhibition of FLJ30927 (Accession NM\_144690). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30927. KIAA1866 (Accession XM\_027658) is another VGAM1903 host target gene. KIAA1866 BINDING SITE is



HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1866, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1866 BINDING SITE, designated SEQ ID:30553, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62890] Another function of VGAM1903 is therefore inhibition of KIAA1866 (Accession XM\_027658). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1866. KIAA1954 (Accession XM\_085375) is another VGAM1903 host target gene. KIAA1954 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1954 BINDING SITE, designated SEQ ID:38094, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62891] Another function of VGAM1903 is therefore inhibition of

KIAA1954 (Accession XM\_085375). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1954. MGC21675 (Accession NM\_052861) is another VGAM1903 host target gene. MGC21675 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC21675, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC21675 BINDING SITE, designated SEQ ID:27442, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62892] Another function of VGAM1903 is therefore inhibition of MGC21675 (Accession NM\_052861). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC21675. TBDN100 (Accession NM\_025085) is another VGAM1903 host target gene. TBDN100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBDN100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of TBDN100 BINDING SITE, designated SEQ ID:24700, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62893] Another function of VGAM1903 is therefore inhibition of TBDN100 (Accession NM\_025085). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBDN100. LOC145815 (Accession XM\_096874) is another VGAM1903 host target gene. LOC145815 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145815, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145815 BINDING SITE, designated SEQ ID:40601, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62894] Another function of VGAM1903 is therefore inhibition of LOC145815 (Accession XM\_096874). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145815. LOC164382 (Accession XM\_104390) is an-

other VGAM1903 host target gene. LOC164382 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164382 BINDING SITE, designated SEQ ID:42162, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62895] Another function of VGAM1903 is therefore inhibition of LOC164382 (Accession XM\_104390). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164382. LOC200169 (Accession XM\_117200) is another VGAM1903 host target gene. LOC200169 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200169, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200169 BINDING SITE, designated SEQ ID:43282, to the nucleotide sequence of VGAM1903 RNA, herein designated VGAM RNA, also designated SEQ ID:4614.

[62896] Another function of VGAM1903 is therefore inhibition of LOC200169 (Accession XM\_117200). Accordingly, utilities of VGAM1903 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200169. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1904 (VGAM1904) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62897] VGAM1904 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1904 was detected is described hereinabove with reference to Figs. 1–8.

[62898] VGAM1904 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Respiratory Syncytial Virus. VGAM1904 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62899] VGAM1904 gene encodes a VGAM1904 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1904 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1904 precursor RNA is designated SEQ ID:1890, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1890 is located at position 8364 relative to the genome of Respiratory Syncytial Virus.

[62900] VGAM1904 precursor RNA folds onto itself, forming VGAM1904 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62901] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1904 folded precursor RNA into VGAM1904 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1904 RNA is designated SEQ ID:4615, and is provided hereinbelow with reference to the sequence listing part.

[62902] VGAM1904 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1904 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1904 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[62903] VGAM1904 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1904 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1904 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1904 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1904 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62904] The complementary binding of VGAM1904 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1904 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1904 host target RNA into VGAM1904 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62905] It is appreciated that VGAM1904 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1904 host target genes. The mRNA of each one of this plurality of VGAM1904 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1904 RNA, herein designated VGAM RNA, and which when bound by VGAM1904 RNA causes inhibition of translation of respective one or more VGAM1904 host target proteins.

[62906] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1904 gene, herein designated VGAM GENE, on one or more VGAM1904 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62907] It is yet further appreciated that a function of VGAM1904 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1904 include diagnosis, prevention and treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGAM1904 correlate with, and may be deduced from, the identity of the host target genes which VGAM1904 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62908] Nucleotide sequences of the VGAM1904 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1904 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1904 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1904 are further described hereinbelow with reference to Table 1.

[62909] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1904 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1904 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[62910] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1904 gene, herein designated VGAM is inhibition of expression of VGAM1904 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1904 correlate with, and may be deduced from, the identity of the target genes which VGAM1904 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62911] FLJ20034 (Accession NM\_017630) is a VGAM1904 host target gene. FLJ20034 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20034 BINDING SITE, designated SEQ ID:19130, to the nucleotide sequence of VGAM1904 RNA, herein designated VGAM RNA, also designated SEQ ID:4615.

[62912] A function of VGAM1904 is therefore inhibition of FLJ20034 (Accession NM\_017630). Accordingly, utilities of VGAM1904 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ20034. KIAA0534 (Accession XM\_049349) is another VGAM1904 host target gene. KIAA0534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0534 BINDING SITE, designated SEQ ID:35379, to the nucleotide sequence of VGAM1904 RNA, herein designated VGAM RNA, also designated SEQ ID:4615.

[62913] Another function of VGAM1904 is therefore inhibition of KIAA0534 (Accession XM\_049349). Accordingly, utilities of VGAM1904 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0534. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1905 (VGAM1905) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62914] VGAM1905 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1905 was detected is described hereinabove with reference to Figs. 1–8.

[62915] VGAM1905 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sendai Virus. VGAM1905 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62916] VGAM1905 gene encodes a VGAM1905 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1905 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1905 precursor RNA is designated SEQ ID:1891, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1891 is located at position 5191 relative to the genome of Sendai Virus.

[62917] VGAM1905 precursor RNA folds onto itself, forming VGAM1905 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62918] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1905 folded precursor RNA into VGAM1905 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 64%) nucleotide sequence of VGAM1905 RNA is designated SEQ ID:4616, and is provided hereinbelow with reference to the sequence listing part.

[62919] VGAM1905 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1905 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1905 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62920] VGAM1905 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1905 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1905 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1905 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1905 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62921] The complementary binding of VGAM1905 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1905 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1905 host target RNA into VGAM1905 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62922] It is appreciated that VGAM1905 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1905 host target genes. The mRNA of each one of this plurality of VGAM1905 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1905 RNA, herein designated VGAM RNA, and which when bound by VGAM1905 RNA causes inhibition of translation of respective one or more VGAM1905 host target proteins.

[62923] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1905 gene, herein designated VGAM GENE, on one or more VGAM1905 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62924] It is yet further appreciated that a function of VGAM1905 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of viral infection by Sendai Virus. Specific functions, and accordingly utilities, of VGAM1905 correlate with, and may be deduced from, the identity of the host target genes which VGAM1905 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62925] Nucleotide sequences of the VGAM1905 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1905 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1905 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1905 are further described hereinbelow with reference to Table 1.

[62926] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1905 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1905 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62927] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1905 gene, herein designated VGAM is inhibition of expression of VGAM1905 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1905 correlate with, and may be deduced from, the identity of the target genes which VGAM1905 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62928] Cockayne Syndrome 1 (classical) (CKN1, Accession NM\_000082) is a VGAM1905 host target gene. CKN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKN1, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKN1 BINDING SITE, designated SEQ ID:5530, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62929] A function of VGAM1905 is therefore inhibition of Cockayne Syndrome 1 (classical) (CKN1, Accession NM\_000082). Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKN1. Pyrimidinergic Receptor P2Y, G-protein Coupled, 6 (P2RY6, Accession NM\_004154) is another VGAM1905 host target gene. P2RY6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P2RY6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RY6 BINDING SITE, designated SEQ ID:10356, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62930] Another function of VGAM1905 is therefore inhibition of Pyrimidinergic Receptor P2Y, G-protein Coupled, 6

(P2RY6, Accession NM\_004154), a gene which mediates cellular responses to nucleotides. Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RY6. The function of P2RY6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM445. Transmembrane Protein 2 (TMEM2, Accession NM\_013390) is another VGAM1905 host target gene. TMEM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TMEM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMEM2 BINDING SITE, designated SEQ ID:15040, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62931] Another function of VGAM1905 is therefore inhibition of Transmembrane Protein 2 (TMEM2, Accession NM\_013390). Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMEM2. Chromosome 13

Open Reading Frame 1 (C13orf1, Accession NM\_020456) is another VGAM1905 host target gene. C13orf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C13orf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C13orf1 BINDING SITE, designated SEQ ID:21692, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62932] Another function of VGAM1905 is therefore inhibition of Chromosome 13 Open Reading Frame 1 (C13orf1, Accession NM\_020456). Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C13orf1. FLJ22390 (Accession NM\_022746) is another VGAM1905 host target gene. FLJ22390 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22390, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22390 BINDING SITE, designated SEQ ID:22956, to the nucleotide sequence of VGAM1905

RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62933] Another function of VGAM1905 is therefore inhibition of FLJ22390 (Accession NM\_022746). Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22390. KIAA0748 (Accession NM\_014796) is another VGAM1905 host target gene. KIAA0748 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0748 BINDING SITE, designated SEQ ID:16699, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62934] Another function of VGAM1905 is therefore inhibition of KIAA0748 (Accession NM\_014796). Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0748. KIAA1317 (Accession XM\_098368) is another VGAM1905 host target gene. KIAA1317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1317 BINDING SITE, designated SEQ ID:41628, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62935] Another function of VGAM1905 is therefore inhibition of KIAA1317 (Accession XM\_098368). Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1317. LOC122792 (Accession NM\_145251) is another VGAM1905 host target gene. LOC122792 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122792, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122792 BINDING SITE, designated SEQ ID:29762, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62936] Another function of VGAM1905 is therefore inhibition of LOC122792 (Accession NM\_145251). Accordingly, utilities

of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122792. LOC148697 (Accession XM\_086276) is another VGAM1905 host target gene. LOC148697 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148697, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148697 BINDING SITE, designated SEQ ID:38571, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62937] Another function of VGAM1905 is therefore inhibition of LOC148697 (Accession XM\_086276). Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148697. LOC221964 (Accession XM\_168342) is another VGAM1905 host target gene. LOC221964 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences



of LOC221964 BINDING SITE, designated SEQ ID:45112, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62938] Another function of VGAM1905 is therefore inhibition of LOC221964 (Accession XM\_168342). Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221964. LOC51134 (Accession NM\_016122) is another VGAM1905 host target gene. LOC51134 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51134 BINDING SITE, designated SEQ ID:18210, to the nucleotide sequence of VGAM1905 RNA, herein designated VGAM RNA, also designated SEQ ID:4616.

[62939] Another function of VGAM1905 is therefore inhibition of LOC51134 (Accession NM\_016122). Accordingly, utilities of VGAM1905 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51134. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1906 (VGAM1906) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62940] VGAM1906 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1906 was detected is described hereinabove with reference to Figs. 1–8.

[62941] VGAM1906 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sendai Virus. VGAM1906 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62942] VGAM1906 gene encodes a VGAM1906 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1906 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1906 precursor RNA is designated SEQ ID:1892, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1892 is located at position 15052 relative to the genome of Sendai Virus.

[62943] VGAM1906 precursor RNA folds onto itself, forming VGAM1906 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62944] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1906 folded precursor RNA into VGAM1906 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1906 RNA is designated SEQ ID:4617, and is provided hereinbelow with reference to the sequence listing part.

[62945] VGAM1906 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1906 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1906 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[62946] VGAM1906 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1906 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1906 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1906 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1906 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62947] The complementary binding of VGAM1906 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1906 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1906 host target RNA into VGAM1906 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62948] It is appreciated that VGAM1906 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1906 host target genes. The mRNA of each one of this plurality of VGAM1906 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1906 RNA, herein designated VGAM RNA, and which when bound by VGAM1906 RNA causes inhibition of translation of respective one or more VGAM1906 host target proteins.

[62949] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1906 gene, herein designated VGAM GENE, on one or more VGAM1906 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62950] It is yet further appreciated that a function of VGAM1906 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1906 include diagnosis, prevention and treatment of viral infection by Sendai Virus. Specific functions, and accordingly utilities, of VGAM1906 correlate with, and may be deduced from, the identity of the host

target genes which VGAM1906 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62951] Nucleotide sequences of the VGAM1906 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1906 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1906 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1906 are further described hereinbelow with reference to Table 1.

[62952] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1906 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1906 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62953] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1906 gene, herein designated VGAM is inhibition of expression of VGAM1906 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1906 correlate with, and may be deduced from, the identity of the target genes which VGAM1906

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62954] Glypican 4 (GPC4, Accession NM\_001448) is a VGAM1906 host target gene. GPC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPC4 BINDING SITE, designated SEQ ID:7178, to the nucleotide sequence of VGAM1906 RNA, herein designated VGAM RNA, also designated SEQ ID:4617.

[62955] A function of VGAM1906 is therefore inhibition of Glypican 4 (GPC4, Accession NM\_001448), a gene which may play a role in growth control and cell division. Accordingly, utilities of VGAM1906 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPC4. The function of GPC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM538.LOC221540 (Accession XM\_168133) is another VGAM1906 host target gene. LOC221540 BINDING SITE is HOST TARGET binding site



found in the 3' untranslated region of mRNA encoded by LOC221540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221540 BINDING SITE, designated SEQ ID:45042, to the nucleotide sequence of VGAM1906 RNA, herein designated VGAM RNA, also designated SEQ ID:4617.

[62956] Another function of VGAM1906 is therefore inhibition of LOC221540 (Accession XM\_168133). Accordingly, utilities of VGAM1906 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221540. LOC257545 (Accession XM\_175217) is another VGAM1906 host target gene. LOC257545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257545 BINDING SITE, designated SEQ ID:46690, to the nucleotide sequence of VGAM1906 RNA, herein designated VGAM RNA, also designated SEQ ID:4617.

[62957] Another function of VGAM1906 is therefore inhibition of

LOC257545 (Accession XM\_175217). Accordingly, utilities of VGAM1906 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257545. LOC257598 (Accession XM\_175295) is another VGAM1906 host target gene. LOC257598 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257598 BINDING SITE, designated SEQ ID:46747, to the nucleotide sequence of VGAM1906 RNA, herein designated VGAM RNA, also designated SEQ ID:4617.

[62958] Another function of VGAM1906 is therefore inhibition of LOC257598 (Accession XM\_175295). Accordingly, utilities of VGAM1906 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257598. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1907 (VGAM1907) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[62959] VGAM1907 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1907 was detected is described hereinabove with reference to Figs. 1–8.

[62960] VGAM1907 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 3. VGAM1907 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62961] VGAM1907 gene encodes a VGAM1907 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1907 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1907 precursor RNA is designated SEQ ID:1893, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1893 is located at position 7040 relative to the genome of Human Parainfluenza Virus 3.

[62962] VGAM1907 precursor RNA folds onto itself, forming VGAM1907 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62963] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1907 folded precursor RNA into VGAM1907 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1907 RNA is designated SEQ ID:4618, and is provided hereinbelow with reference to the sequence listing part.

[62964] VGAM1907 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1907 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1907 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[62965] VGAM1907 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1907 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1907 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1907 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1907 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[62966] The complementary binding of VGAM1907 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1907 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1907 host target RNA into VGAM1907 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62967] It is appreciated that VGAM1907 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1907 host target genes. The mRNA of each one of this plurality of VGAM1907 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1907 RNA, herein designated VGAM RNA, and which when bound by VGAM1907 RNA causes inhibition of translation of respective one or more VGAM1907 host target proteins.

[62968] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1907 gene, herein designated VGAM GENE, on one

or more VGAM1907 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62969] It is yet further appreciated that a function of VGAM1907 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1907 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGAM1907 correlate with, and may be deduced from, the identity of the host target genes which VGAM1907 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62970] Nucleotide sequences of the VGAM1907 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1907 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1907 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1907 are further described hereinbelow with reference to Table 1.

[62971] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1907 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1907 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62972] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1907 gene, herein designated VGAM is inhibition of expression of VGAM1907 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1907 correlate with, and may be deduced from, the identity of the target genes which VGAM1907 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62973] KIAA0471 (Accession NM\_014857) is a VGAM1907 host



target gene. KIAA0471 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0471 BINDING SITE, designated SEQ ID:16910, to the nucleotide sequence of VGAM1907 RNA, herein designated VGAM RNA, also designated SEQ ID:4618.

[62974] A function of VGAM1907 is therefore inhibition of KIAA0471 (Accession NM\_014857). Accordingly, utilities of VGAM1907 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0471. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1908 (VGAM1908) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[62975] VGAM1908 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1908 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[62976] VGAM1908 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 3. VGAM1908 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[62977] VGAM1908 gene encodes a VGAM1908 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1908 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1908 precursor RNA is designated SEQ ID:1894, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1894 is located at position 8620 relative to the genome of Human Parainfluenza Virus 3.

[62978] VGAM1908 precursor RNA folds onto itself, forming VGAM1908 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[62979] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1908 folded precursor RNA into VGAM1908 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1908 RNA is designated SEQ ID:4619, and is provided hereinbelow with reference to the sequence listing part.

[62980] VGAM1908 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1908 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1908 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[62981] VGAM1908 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1908 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1908 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1908 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1908 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[62982] The complementary binding of VGAM1908 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1908 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1908 host target RNA into VGAM1908 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[62983] It is appreciated that VGAM1908 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1908 host target genes. The mRNA of each one of this plurality of VGAM1908 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1908 RNA, herein designated VGAM RNA, and which when bound by VGAM1908 RNA causes inhibition of translation of respective one or more VGAM1908 host target proteins.

[62984] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1908 gene, herein designated VGAM GENE, on one or more VGAM1908 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[62985] It is yet further appreciated that a function of VGAM1908 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1908 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGAM1908 correlate with, and may be deduced from, the identity of the host target genes which VGAM1908 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[62986] Nucleotide sequences of the VGAM1908 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1908 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1908 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1908 are further described hereinbelow with reference to Table 1.

[62987] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1908 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1908 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[62988] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1908 gene, herein designated VGAM is inhibition of expression of VGAM1908 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1908 correlate with, and may be deduced from, the identity of the target genes which VGAM1908 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[62989] Solute Carrier Family 29 (nucleoside transporters), Member 1 (SLC29A1, Accession NM\_004955) is a VGAM1908 host target gene. SLC29A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC29A1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC29A1 BINDING SITE, designated SEQ ID:11401, to the nucleotide sequence of VGAM1908 RNA, herein designated VGAM RNA, also designated SEQ ID:4619.

[62990] A function of VGAM1908 is therefore inhibition of Solute Carrier Family 29 (nucleoside transporters), Member 1 (SLC29A1, Accession NM\_004955), a gene which mediates both influx and efflux of nucleosides across the membrane. Accordingly, utilities of VGAM1908 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC29A1. The function of SLC29A1 has been established by previous studies. An essential component of the action of nucleoside analog drugs used in anticancer therapies is the mediated uptake of the drug across the plasma membrane and into the cell. This is achieved by integral membrane proteins known as nucleoside transporters. There are 2 major families of nucleoside transporters, the concentrative and the equilibrative. The concentrative nucleoside transporters appear to be restricted in their distribution within cells and tissues and also in their selectivity of nucleoside permeants. In con-



trast, the equilibrative nucleoside transporters appear to be widely distributed and have a broad substrate specificity. Griffiths et al. (1997) cloned the cDNA for the prototypic equilibrative transporter ENT1 from human placenta. Choi et al. (2000) cloned and sequenced the mouse Ent1 gene. Northern blot analysis detected expression of Ent1 in all tissues except skeletal muscle, with highest levels in liver, heart, testis, spleen, lung, kidney, and brain.

[62991] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[62992] Griffiths, M.; Beaumont, N.; Yao, S. Y. M.; Sundaram, M.; Boumah, C. E.; Davies, A.; Kwong, F. Y. P.; Coe, I.; Cass, C. E.; Young, J. D.; Baldwin, S. A. : Cloning of a human nucleoside transporter implicated in the cellular uptake of adenosine and chemotherapeutic drugs. *Nature Med.* 3: 89–94, 1997. ; and

[62993] Choi, D.-S.; Handa, M.; Young, H.; Gordon, A. S.; Diamond, I.; Messing, R. O. : Genomic organization and expression of the mouse equilibrative, nitrobenzylthioinosine-sensitive nucleoside.

[62994] Further studies establishing the function and utilities of

SLC29A1 are found in John Hopkins OMIM database record ID 602193, and in cited publications numbered 5854–5856 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Steroid Sulfatase (microsomal), Arylsulfatase C, Isozyme S (STS, Accession NM\_000351) is another VGAM1908 host target gene. STS BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STS BINDING SITE, designated SEQ ID:5912, to the nucleotide sequence of VGAM1908 RNA, herein designated VGAM RNA, also designated SEQ ID:4619.

[62995] Another function of VGAM1908 is therefore inhibition of Steroid Sulfatase (microsomal), Arylsulfatase C, Isozyme S (STS, Accession NM\_000351). Accordingly, utilities of VGAM1908 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STS. KIAA0543 (Accession XM\_044213) is another VGAM1908 host target gene. KIAA0543 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0543, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0543 BINDING SITE, designated SEQ ID:34179, to the nucleotide sequence of VGAM1908 RNA, herein designated VGAM RNA, also designated SEQ ID:4619.

[62996] Another function of VGAM1908 is therefore inhibition of KIAA0543 (Accession XM\_044213). Accordingly, utilities of VGAM1908 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0543. UMP-CMPK (Accession NM\_016308) is another VGAM1908 host target gene. UMP-CMPK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UMP-CMPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UMP-CMPK BINDING SITE, designated SEQ ID:18427, to the nucleotide sequence of VGAM1908 RNA, herein designated VGAM RNA, also designated SEQ ID:4619.

[62997] Another function of VGAM1908 is therefore inhibition of UMP-CMPK (Accession NM\_016308). Accordingly, utilities of VGAM1908 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with UMP-CMPK. LOC152441 (Accession XM\_098230) is another VGAM1908 host target gene. LOC152441 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC152441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152441 BINDING SITE, designated SEQ ID:41507, to the nucleotide sequence of VGAM1908 RNA, herein designated VGAM RNA, also designated SEQ ID:4619.

[62998] Another function of VGAM1908 is therefore inhibition of LOC152441 (Accession XM\_098230). Accordingly, utilities of VGAM1908 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152441. LOC51313 (Accession NM\_016613) is another VGAM1908 host target gene. LOC51313 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51313 BINDING SITE, designated SEQ ID:18721, to the

nucleotide sequence of VGAM1908 RNA, herein designated VGAM RNA, also designated SEQ ID:4619.

[62999] Another function of VGAM1908 is therefore inhibition of LOC51313 (Accession NM\_016613). Accordingly, utilities of VGAM1908 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51313. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1909 (VGAM1909) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63000] VGAM1909 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1909 was detected is described hereinabove with reference to Figs. 1–8.

[63001] VGAM1909 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 3. VGAM1909 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63002] VGAM1909 gene encodes a VGAM1909 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1909 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1909 precursor RNA is designated SEQ ID:1895, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1895 is located at position 5850 relative to the genome of Human Parainfluenza Virus 3.

[63003] VGAM1909 precursor RNA folds onto itself, forming VGAM1909 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63004] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1909 folded precursor RNA into VGAM1909 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1909 RNA is designated SEQ ID:4620, and is provided hereinbelow with reference to the sequence listing part.

[63005] VGAM1909 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1909 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1909 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63006] VGAM1909 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1909 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1909 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1909 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1909 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63007] The complementary binding of VGAM1909 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1909 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1909 host target RNA into VGAM1909 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63008] It is appreciated that VGAM1909 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM1909 host target genes. The mRNA of each one of this plurality of VGAM1909 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1909 RNA, herein designated VGAM RNA, and which when bound by VGAM1909 RNA causes inhibition of translation of respective one or more VGAM1909 host target proteins.

[63009] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1909 gene, herein designated VGAM GENE, on one or more VGAM1909 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[63010] It is yet further appreciated that a function of VGAM1909 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGAM1909 correlate with, and may be deduced from, the identity of the host target genes which VGAM1909 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63011] Nucleotide sequences of the VGAM1909 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1909 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1909 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1909 are further described hereinbelow with reference to Table 1.

[63012] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1909 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1909 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63013] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1909 gene, herein designated VGAM is inhibition of expression of VGAM1909 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1909 correlate with, and may be deduced from, the identity of the target genes which VGAM1909 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63014] High Mobility Group AT-hook 2 (HMGA2, Accession NM\_003483) is a VGAM1909 host target gene. HMGA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGA2 BINDING SITE, designated SEQ ID:9560, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63015] A function of VGAM1909 is therefore inhibition of High Mobility Group AT-hook 2 (HMGA2, Accession

NM\_003483), a gene which may affect transcription and cell differentiation; shares common DNA-binding motif with other HMG HMG I/Y family members. Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGA2. The function of HMGA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Myelin Protein Zero (Charcot-Marie-Tooth neuropathy 1B) (MPZ, Accession NM\_000530) is another VGAM1909 host target gene. MPZ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPZ BINDING SITE, designated SEQ ID:6129, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63016] Another function of VGAM1909 is therefore inhibition of Myelin Protein Zero (Charcot-Marie-Tooth neuropathy 1B) (MPZ, Accession NM\_000530). Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MPZ. Nucleoporin 98kDa (NUP98, Accession NM\_016320) is another VGAM1909 host target gene. NUP98 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NUP98, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUP98 BINDING SITE, designated SEQ ID:18438, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63017] Another function of VGAM1909 is therefore inhibition of Nucleoporin 98kDa (NUP98, Accession NM\_016320), a gene which functions in the nuclear transport of protein and RNA. Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUP98. The function of NUP98 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.FLJ20232 (Accession NM\_019008) is another VGAM1909 host target gene. FLJ20232 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded

by FLJ20232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20232 BINDING SITE, designated SEQ ID:21081, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63018] Another function of VGAM1909 is therefore inhibition of FLJ20232 (Accession NM\_019008). Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20232. FLJ32389 (Accession NM\_144617) is another VGAM1909 host target gene. FLJ32389 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32389, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32389 BINDING SITE, designated SEQ ID:29433, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63019] Another function of VGAM1909 is therefore inhibition of FLJ32389 (Accession NM\_144617). Accordingly, utilities of

VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32389. KIAA1855 (Accession XM\_166453) is another VGAM1909 host target gene. KIAA1855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1855 BINDING SITE, designated SEQ ID:44351, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63020] Another function of VGAM1909 is therefore inhibition of KIAA1855 (Accession XM\_166453). Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1855. LOC144231 (Accession XM\_096561) is another VGAM1909 host target gene. LOC144231 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC144231 BINDING SITE, designated SEQ ID:40391, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63021] Another function of VGAM1909 is therefore inhibition of LOC144231 (Accession XM\_096561). Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144231. LOC161823 (Accession XM\_091156) is another VGAM1909 host target gene. LOC161823 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC161823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161823 BINDING SITE, designated SEQ ID:40034, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63022] Another function of VGAM1909 is therefore inhibition of LOC161823 (Accession XM\_091156). Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161823. LOC201191 (Accession XM\_117058) is another VGAM1909 host target gene. LOC201191 BINDING



SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201191 BINDING SITE, designated SEQ ID:43214, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63023] Another function of VGAM1909 is therefore inhibition of LOC201191 (Accession XM\_117058). Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201191. LOC220776 (Accession XM\_043388) is another VGAM1909 host target gene. LOC220776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220776 BINDING SITE, designated SEQ ID:33931, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63024] Another function of VGAM1909 is therefore inhibition of

LOC220776 (Accession XM\_043388). Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220776. LOC91409 (Accession XM\_038298) is another VGAM1909 host target gene. LOC91409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91409 BINDING SITE, designated SEQ ID:32802, to the nucleotide sequence of VGAM1909 RNA, herein designated VGAM RNA, also designated SEQ ID:4620.

[63025] Another function of VGAM1909 is therefore inhibition of LOC91409 (Accession XM\_038298). Accordingly, utilities of VGAM1909 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91409. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1910 (VGAM1910) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[63026] VGAM1910 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1910 was detected is described hereinabove with reference to Figs. 1–8.

[63027] VGAM1910 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 3. VGAM1910 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63028] VGAM1910 gene encodes a VGAM1910 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1910 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1910 precursor RNA is designated SEQ ID:1896, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1896 is located at position 8937 relative to the genome of Human Parainfluenza Virus 3.

[63029] VGAM1910 precursor RNA folds onto itself, forming VGAM1910 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63030] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1910 folded precursor RNA into VGAM1910 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1910 RNA is designated SEQ ID:4621, and is provided hereinbelow with reference to the sequence listing part.

[63031] VGAM1910 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1910 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1910 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[63032] VGAM1910 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1910 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1910 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1910 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1910 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[63033] The complementary binding of VGAM1910 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1910 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1910 host target RNA into VGAM1910 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63034] It is appreciated that VGAM1910 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1910 host target genes. The mRNA of each one of this plurality of VGAM1910 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1910 RNA, herein designated VGAM RNA, and which when bound by VGAM1910 RNA causes inhibition of translation of respective one or more VGAM1910 host target proteins.

[63035] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1910 gene, herein designated VGAM GENE, on one

or more VGAM1910 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63036] It is yet further appreciated that a function of VGAM1910 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1910 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGAM1910 correlate with, and may be deduced from, the identity of the host target genes which VGAM1910 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63037] Nucleotide sequences of the VGAM1910 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1910 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1910 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1910 are further described hereinbelow with reference to Table 1.

[63038] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1910 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1910 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63039] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1910 gene, herein designated VGAM is inhibition of expression of VGAM1910 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1910 correlate with, and may be deduced from, the identity of the target genes which VGAM1910 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63040] Fibronectin Leucine Rich Transmembrane Protein 2



(FLRT2, Accession NM\_013231) is a VGAM1910 host target gene. FLRT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14884, to the nucleotide sequence of VGAM1910 RNA, herein designated VGAM RNA, also designated SEQ ID:4621.

[63041] A function of VGAM1910 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM\_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM1910 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Folate Receptor 1 (adult) (FOLR1, Accession NM\_016730) is another VGAM1910 host target gene. FOLR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

FOLR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOLR1 BINDING SITE, designated SEQ ID:18783, to the nucleotide sequence of VGAM1910 RNA, herein designated VGAM RNA, also designated SEQ ID:4621.

[63042] Another function of VGAM1910 is therefore inhibition of Folate Receptor 1 (adult) (FOLR1, Accession NM\_016730), a gene which binds and initiates transport of folate and methotrexate. Accordingly, utilities of VGAM1910 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOLR1. The function of FOLR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM399. Lipin 1 (LPIN1, Accession XM\_041136) is another VGAM1910 host target gene. LPIN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPIN1 BIND-

ING SITE, designated SEQ ID:33464, to the nucleotide sequence of VGAM1910 RNA, herein designated VGAM RNA, also designated SEQ ID:4621.

[63043] Another function of VGAM1910 is therefore inhibition of Lipin 1 (LPIN1, Accession XM\_041136), a gene which is involved in adipocyte differentiation (by similarity). Accordingly, utilities of VGAM1910 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPIN1. The function of LPIN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM35. Phosphatidylinositol Transfer Protein, Beta (PITPNB, Accession NM\_012399) is another VGAM1910 host target gene. PITPNB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PITPNB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PITPNB BINDING SITE, designated SEQ ID:14765, to the nucleotide sequence of VGAM1910 RNA, herein designated VGAM RNA, also designated SEQ ID:4621.

[63044] Another function of VGAM1910 is therefore inhibition of

Phosphatidylinositol Transfer Protein, Beta (PITPNB, Accession NM\_012399), a gene which catalyzes the transfer of ptdins and phosphatidylcholine between membranes. Accordingly, utilities of VGAM1910 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PITPNB. The function of PITPNB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1016. EDR1 (Accession NM\_004426) is another VGAM1910 host target gene. EDR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EDR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDR1 BINDING SITE, designated SEQ ID:10701, to the nucleotide sequence of VGAM1910 RNA, herein designated VGAM RNA, also designated SEQ ID:4621.

[63045] Another function of VGAM1910 is therefore inhibition of EDR1 (Accession NM\_004426). Accordingly, utilities of VGAM1910 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDR1. FLJ10201 (Accession NM\_018023) is another VGAM1910

host target gene. FLJ10201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10201 BINDING SITE, designated SEQ ID:19763, to the nucleotide sequence of VGAM1910 RNA, herein designated VGAM RNA, also designated SEQ ID:4621.

[63046] Another function of VGAM1910 is therefore inhibition of FLJ10201 (Accession NM\_018023). Accordingly, utilities of VGAM1910 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10201. KIAA1350 (Accession XM\_052597) is another VGAM1910 host target gene. KIAA1350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1350 BINDING SITE, designated SEQ ID:35999, to the nucleotide sequence of VGAM1910 RNA, herein designated VGAM RNA, also designated SEQ ID:4621.

[63047] Another function of VGAM1910 is therefore inhibition of KIAA1350 (Accession XM\_052597). Accordingly, utilities of VGAM1910 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1350. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1911 (VGAM1911) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63048] VGAM1911 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1911 was detected is described hereinabove with reference to Figs. 1–8.

[63049] VGAM1911 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 3. VGAM1911 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63050] VGAM1911 gene encodes a VGAM1911 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1911 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1911 precursor RNA is designated SEQ ID:1897, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1897 is located at position 1061 relative to the genome of Human Parainfluenza Virus 3.

[63051] VGAM1911 precursor RNA folds onto itself, forming VGAM1911 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63052] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1911 folded precursor RNA into VGAM1911 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1911 RNA is designated SEQ ID:4622, and is provided hereinbelow with reference to the sequence listing part.

[63053] VGAM1911 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1911 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1911 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[63054] VGAM1911 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1911 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1911 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the



number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1911 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1911 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63055] The complementary binding of VGAM1911 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1911 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1911 host target RNA into VGAM1911 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63056] It is appreciated that VGAM1911 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1911 host target genes. The mRNA of each one of this plurality of VGAM1911 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1911 RNA, herein designated VGAM RNA, and which when bound by VGAM1911 RNA causes inhibition of translation of respective one or more VGAM1911 host target proteins.

[63057] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1911 gene, herein designated VGAM GENE, on one or more VGAM1911 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63058] It is yet further appreciated that a function of VGAM1911 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGAM1911 correlate with, and may be deduced from, the identity of the host target genes which VGAM1911 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63059] Nucleotide sequences of the VGAM1911 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1911 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1911 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1911 are further described hereinbelow with reference to Table 1.

[63060] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1911 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1911 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[63061] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1911 gene, herein designated VGAM is inhibition of expression of VGAM1911 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1911 correlate with, and may be deduced from, the identity of the target genes which VGAM1911 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63062] Breast Cancer 1, Early Onset (BRCA1, Accession NM\_007294) is a VGAM1911 host target gene. BRCA1 BINDING SITE1 through BRCA1 BINDING SITE10 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BRCA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRCA1 BINDING SITE1 through BRCA1 BINDING SITE10, designated SEQ ID:14166, SEQ ID:14172, SEQ ID:14178, SEQ ID:14185, SEQ ID:14191, SEQ ID:14197, SEQ ID:14205, SEQ ID:14211, SEQ ID:14217 and SEQ ID:14223 respectively, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63063] A function of VGAM1911 is therefore inhibition of Breast Cancer 1, Early Onset (BRCA1, Accession NM\_007294). Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRCA1. Carbonic Anhydrase III, Muscle Specific (CA3, Accession NM\_005181) is another VGAM1911 host target gene. CA3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CA3 BINDING SITE, designated SEQ ID:11680, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63064] Another function of VGAM1911 is therefore inhibition of Carbonic Anhydrase III, Muscle Specific (CA3, Accession NM\_005181), a gene which has a muscle-specific function of reversible hydration of carbon dioxide. Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CA3. The function of CA3 has been established by previous studies. Carbonic anhydrases (CAs) are a family

of zinc metalloenzymes. Carbonic anhydrase III is found in high concentration in muscle. It shows relatively poor hydratase and esterase activities compared to the red cell isozymes CA I (OMIM Ref. No. 114800) and CA II (OMIM Ref. No. 259730), but is similar in subunit structure (monomer) and molecular mass (28 kD). Heath et al. (1985) explored the use of CA III in conjunction with creatine kinase detection of the carrier state for Duchenne muscular dystrophy.

[63065] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63066] Heath, R.; Carter, N. D.; Jeffery, S.; Edwards, R. J.; Watts, D. C.; Watts, R. L. : Evaluation of carrier detection of Duchenne muscular dystrophy using carbonic anhydrase III and creatine kinase. Am. J. Med. Genet. 21: 291–296, 1985. ; and

[63067] Edwards, Y. H.; Lloyd, J. C.; Parkar, M.; Povey, S. : The gene for human muscle specific carbonic anhydrase (CAIII) is assigned to chromosome 8. Ann. Hum. Genet. 50: 41–47, 1986.

[63068] Further studies establishing the function and utilities of CA3 are found in John Hopkins OMIM database record ID

114750, and in cited publications numbered 3710–371 and 11874 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 16 (lymphocyte chemoattractant factor) (IL16, Accession NM\_004513) is another VGAM1911 host target gene. IL16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL16 BINDING SITE, designated SEQ ID:10841, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63069] Another function of VGAM1911 is therefore inhibition of Interleukin 16 (lymphocyte chemoattractant factor) (IL16, Accession NM\_004513), a gene which modulates T-cell activation. Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL16. The function of IL16 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

## VGAM819.Meningioma Expressed Antigen 5

(hyaluronidase) (MGEA5, Accession NM\_012215) is another VGAM1911 host target gene. MGEA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGEA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGEA5 BINDING SITE, designated SEQ ID:14520, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63070] Another function of VGAM1911 is therefore inhibition of Meningioma Expressed Antigen 5 (hyaluronidase) (MGEA5, Accession NM\_012215), a gene which has a hyaluronidase activity. Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGEA5. The function of MGEA5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM801.Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM\_031409) is another VGAM1911 host target gene. CCR6 BINDING SITE is HOST TARGET binding site



found in the 5' untranslated region of mRNA encoded by CCR6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR6 BINDING SITE, designated SEQ ID:25375, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63071] Another function of VGAM1911 is therefore inhibition of Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM\_031409). Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR6. DJ167A19.1 (Accession NM\_018982) is another VGAM1911 host target gene. DJ167A19.1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ167A19.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ167A19.1 BINDING SITE, designated SEQ ID:21052, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63072] Another function of VGAM1911 is therefore inhibition of

DJ167A19.1 (Accession NM\_018982). Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ167A19.1. FLJ10579 (Accession NM\_018145) is another VGAM1911 host target gene. FLJ10579 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10579, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10579 BINDING SITE, designated SEQ ID:19946, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63073] Another function of VGAM1911 is therefore inhibition of FLJ10579 (Accession NM\_018145). Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10579. FLJ10829 (Accession NM\_018234) is another VGAM1911 host target gene. FLJ10829 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10829, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ10829 BINDING SITE, designated SEQ ID:20181, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63074] Another function of VGAM1911 is therefore inhibition of FLJ10829 (Accession NM\_018234). Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10829. FLJ23462 (Accession NM\_024843) is another VGAM1911 host target gene. FLJ23462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23462 BINDING SITE, designated SEQ ID:24267, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63075] Another function of VGAM1911 is therefore inhibition of FLJ23462 (Accession NM\_024843). Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23462. KIAA0285 (Accession NM\_014807) is another

VGAM1911 host target gene. KIAA0285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0285 BINDING SITE, designated SEQ ID:16756, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63076] Another function of VGAM1911 is therefore inhibition of KIAA0285 (Accession NM\_014807). Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0285. SEC15B (Accession XM\_039570) is another VGAM1911 host target gene. SEC15B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC15B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC15B BINDING SITE, designated SEQ ID:33129, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63077] Another function of VGAM1911 is therefore inhibition of SEC15B (Accession XM\_039570). Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC15B. LOC197131 (Accession XM\_113823) is another VGAM1911 host target gene. LOC197131 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197131 BINDING SITE, designated SEQ ID:42449, to the nucleotide sequence of VGAM1911 RNA, herein designated VGAM RNA, also designated SEQ ID:4622.

[63078] Another function of VGAM1911 is therefore inhibition of LOC197131 (Accession XM\_113823). Accordingly, utilities of VGAM1911 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197131. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1912 (VGAM1912) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[63079] VGAM1912 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1912 was detected is described hereinabove with reference to Figs. 1–8.

[63080] VGAM1912 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 3. VGAM1912 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63081] VGAM1912 gene encodes a VGAM1912 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1912 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1912 precursor RNA is designated SEQ ID:1898, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1898 is located at position 12367 relative to the genome of Human Parainfluenza Virus 3.

[63082] VGAM1912 precursor RNA folds onto itself, forming VGAM1912 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63083] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1912 folded precursor RNA into VGAM1912 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide sequence of VGAM1912 RNA is designated SEQ ID:4623, and is provided hereinbelow with reference to the sequence listing part.

[63084] VGAM1912 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1912 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1912 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63085] VGAM1912 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1912 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1912 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1912 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1912 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in



the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63086] The complementary binding of VGAM1912 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1912 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1912 host target RNA into VGAM1912 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63087] It is appreciated that VGAM1912 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1912 host target genes. The mRNA of each one of this plurality of VGAM1912 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1912 RNA, herein designated VGAM RNA, and which when bound by VGAM1912 RNA causes inhibition of translation of respective one or more VGAM1912 host target proteins.

[63088] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1912 gene, herein designated VGAM GENE, on one or more VGAM1912 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63089] It is yet further appreciated that a function of VGAM1912 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGAM1912 correlate with, and may be deduced from, the identity of the host target genes which VGAM1912 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[63090] Nucleotide sequences of the VGAM1912 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1912 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1912 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1912 are further described hereinbelow with reference to Table 1.

[63091] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1912 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1912 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63092] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1912 gene, herein designated VGAM is inhibition of expression of VGAM1912 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1912 correlate with, and may be deduced from, the identity of the target genes which VGAM1912 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63093] Cyclin-dependent Kinase Inhibitor 1A (p21, Cip1)

(CDKN1A, Accession NM\_078467) is a VGAM1912 host target gene. CDKN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDKN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN1A BINDING SITE, designated SEQ ID:27783, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63094] A function of VGAM1912 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 1A (p21, Cip1) (CDKN1A, Accession NM\_078467), a gene which inhibits cyclin-kinase activity and probably serves as the effector of p53 cell cycle control. Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN1A. The function of CDKN1A has been established by previous studies. The preferred name and symbol for this gene are cyclin-dependent kinase inhibitor-1A (OMIM Ref. No. CDKN1A). Also referred to as p21 and as CDKN1, this protein inhibits cyclin-kinase activity, is tightly regulated at the

transcriptional level by p53, and probably serves as the effector of p53 cell cycle control. The ability of p53 (OMIM Ref. No. 191170) to activate transcription from specific sequences suggests that genes induced by p53 may mediate its biologic role as a tumor suppressor. Using a subtractive hybridization approach, El-Deiry et al. (1993) identified a gene they called WAF1 (for wildtype p53-activated fragment 1), whose induction was associated with wildtype but not mutant p53 gene expression in a human brain tumor cell line. El-Deiry et al. (1993) found that the sequence, structure, and activation by p53 was conserved in rodents. Introduction of WAF1 cDNA suppressed the growth of human brain, lung, and colon tumor cells in culture. Using a yeast enhancer trap, they identified a p53-binding site 2.4 kb upstream of WAF1 coding sequences. The WAF1 promoter, including this p53-binding site, conferred p53-dependent inducibility upon a heterologous reporter gene. After acceptance of their paper for publication, El-Deiry et al. (1993) learned that Harper et al. (1993) had identified a gene, called CIP1, whose product binds to cyclin complexes and inhibits the function of cyclin-dependent kinases. They found that the sequence of CIP1, described by Harper et

al. (1993) in the same issue of Cell, was identical to that of WAF1. The results provided a dramatic example of the interplay between tumor suppressor genes and the cell cycle.

[63095] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63096] El-Deiry, W. S.; Tokino, T.; Velculescu, V. E.; Levy, D. B.; Parsons, R.; Trent, J. M.; Lin, D.; Mercer, E.; Kinzler, K. W.; Vogelstein, B. : WAF1, a potential mediator of p53 tumor suppression. Cell 75: 817–825, 1993. ; and

[63097] Harper, J. W.; Adami, G. R.; Wei, N.; Keyomarsi, K.; Elledge, S. J. : The p21 Cdk-interacting protein Cip1 is a potent inhibitor of G1 cyclin-dependent kinases. Cell 75: 805–816, 1993.

[63098] Further studies establishing the function and utilities of CDKN1A are found in John Hopkins OMIM database record ID 116899, and in cited publications numbered 4130, 9827–4132, 4342, 10700–4134, 7124–4136, 2969, 1276 and 3140 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome Condensation 1-like (CHC1L, Accession NM\_001268) is another VGAM1912 host target gene.

CHC1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHC1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHC1L BINDING SITE, designated SEQ ID:6930, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63099] Another function of VGAM1912 is therefore inhibition of Chromosome Condensation 1-like (CHC1L, Accession NM\_001268). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHC1L. EGF-containing Fibulin-like Extracellular Matrix Protein 1 (EFEMP1, Accession NM\_004105) is another VGAM1912 host target gene. EFEMP1 BINDING SITE1 and EFEMP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by EFEMP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFEMP1 BINDING SITE1 and EFEMP1 BINDING SITE2, designated SEQ

ID:10318 and SEQ ID:20838 respectively, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63100] Another function of VGAM1912 is therefore inhibition of EGF-containing Fibulin-like Extracellular Matrix Protein 1 (EFEMP1, Accession NM\_004105). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFEMP1. Potassium Voltage-gated Channel, Shaker-related Subfamily, Beta Member 1 (KCNAB1, Accession XM\_027634) is another VGAM1912 host target gene. KCNAB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNAB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNAB1 BINDING SITE, designated SEQ ID:30548, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63101] Another function of VGAM1912 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Beta Member 1 (KCNAB1, Accession XM\_027634), a



gene which is the regulatory beta subunit for a shaker-related voltage-gated potassium channel. Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNAB1. The function of KCNAB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM727. RecQ Protein-like 5 (RECQL5, Accession NM\_004259) is another VGAM1912 host target gene. RECQL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RECQL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RECQL5 BINDING SITE, designated SEQ ID:10450, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63102] Another function of VGAM1912 is therefore inhibition of RecQ Protein-like 5 (RECQL5, Accession NM\_004259). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RECQL5. Solute Carrier Family 4, Sodium

Bicarbonate Transporter-like, Member 10 (SLC4A10, Accession NM\_022058) is another VGAM1912 host target gene. SLC4A10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC4A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A10 BINDING SITE, designated SEQ ID:22595, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63103] Another function of VGAM1912 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Transporter-like, Member 10 (SLC4A10, Accession NM\_022058). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A10. Vasoactive Intestinal Peptide Receptor 1 (VIPR1, Accession NM\_004624) is another VGAM1912 host target gene. VIPR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VIPR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of VIPR1 BINDING SITE, designated SEQ ID:10993, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63104] Another function of VGAM1912 is therefore inhibition of Vasoactive Intestinal Peptide Receptor 1 (VIPR1, Accession NM\_004624), a gene which binds vip and is mediated by g proteins which activate adenylyl cyclase. Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIPR1. The function of VIPR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM548. Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM\_041375) is another VGAM1912 host target gene. C6orf37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf37 BINDING SITE, designated SEQ ID:33515, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM

RNA, also designated SEQ ID:4623.

[63105] Another function of VGAM1912 is therefore inhibition of Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM\_041375). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf37. Coenzyme Q7 Homolog, Ubiquinone (yeast) (COQ7, Accession NM\_016138) is another VGAM1912 host target gene. COQ7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COQ7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COQ7 BINDING SITE, designated SEQ ID:18224, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63106] Another function of VGAM1912 is therefore inhibition of Coenzyme Q7 Homolog, Ubiquinone (yeast) (COQ7, Accession NM\_016138). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COQ7. DKFZP434B172 (Accession XM\_046264) is another VGAM1912 host target gene. DKFZP434B172 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434B172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434B172 BINDING SITE, designated SEQ ID:34703, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63107] Another function of VGAM1912 is therefore inhibition of DKFZP434B172 (Accession XM\_046264). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434B172. DKFZP564D0462 (Accession XM\_047080) is another VGAM1912 host target gene. DKFZP564D0462 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564D0462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564D0462 BINDING SITE, designated SEQ ID:34898, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4623.

[63108] Another function of VGAM1912 is therefore inhibition of DKFZP564D0462 (Accession XM\_047080). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D0462. FLJ12707 (Accession NM\_022067) is another VGAM1912 host target gene. FLJ12707 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12707, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12707 BINDING SITE, designated SEQ ID:22610, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63109] Another function of VGAM1912 is therefore inhibition of FLJ12707 (Accession NM\_022067). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12707. FLJ20081 (Accession NM\_017658) is another VGAM1912 host target gene. FLJ20081 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20081, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20081 BINDING SITE, designated SEQ ID:19181, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63110] Another function of VGAM1912 is therefore inhibition of FLJ20081 (Accession NM\_017658). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20081. FLJ23499 (Accession NM\_022761) is another VGAM1912 host target gene. FLJ23499 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23499 BINDING SITE, designated SEQ ID:23006, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63111] Another function of VGAM1912 is therefore inhibition of FLJ23499 (Accession NM\_022761). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ23499. KIAA0759 (Accession XM\_041090) is another VGAM1912 host target gene. KIAA0759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0759 BINDING SITE, designated SEQ ID:33442, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63112] Another function of VGAM1912 is therefore inhibition of KIAA0759 (Accession XM\_041090). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0759. KIAA1908 (Accession XM\_055834) is another VGAM1912 host target gene. KIAA1908 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1908 BINDING SITE, designated SEQ ID:36337, to the



nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63113] Another function of VGAM1912 is therefore inhibition of KIAA1908 (Accession XM\_055834). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1908. Mitogen-activated Protein Kinase Kinase Kinase 2 (MAP3K2, Accession NM\_006609) is another VGAM1912 host target gene. MAP3K2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K2 BINDING SITE, designated SEQ ID:13385, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63114] Another function of VGAM1912 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 2 (MAP3K2, Accession NM\_006609). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K2. PP1665 (Accession NM\_030792) is another

VGAM1912 host target gene. PP1665 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PP1665, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP1665 BINDING SITE, designated SEQ ID:25094, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63115] Another function of VGAM1912 is therefore inhibition of PP1665 (Accession NM\_030792). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP1665. PRO1728 (Accession NM\_018505) is another VGAM1912 host target gene. PRO1728 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1728, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1728 BINDING SITE, designated SEQ ID:20571, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63116] Another function of VGAM1912 is therefore inhibition of PRO1728 (Accession NM\_018505). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1728. LOC134266 (Accession XM\_059701) is another VGAM1912 host target gene. LOC134266 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC134266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134266 BINDING SITE, designated SEQ ID:37073, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63117] Another function of VGAM1912 is therefore inhibition of LOC134266 (Accession XM\_059701). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134266. LOC158314 (Accession XM\_098920) is another VGAM1912 host target gene. LOC158314 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC158314, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158314 BINDING SITE, designated SEQ ID:41955, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63118] Another function of VGAM1912 is therefore inhibition of LOC158314 (Accession XM\_098920). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158314. LOC90643 (Accession XM\_033145) is another VGAM1912 host target gene. LOC90643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90643 BINDING SITE, designated SEQ ID:31856, to the nucleotide sequence of VGAM1912 RNA, herein designated VGAM RNA, also designated SEQ ID:4623.

[63119] Another function of VGAM1912 is therefore inhibition of LOC90643 (Accession XM\_033145). Accordingly, utilities of VGAM1912 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90643. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1913 (VGAM1913) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63120] VGAM1913 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1913 was detected is described hereinabove with reference to Figs. 1–8.

[63121] VGAM1913 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 3. VGAM1913 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63122] VGAM1913 gene encodes a VGAM1913 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1913 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1913 precursor RNA is designated SEQ ID:1899, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1899 is located at position 8166 relative to the genome of Human Parainfluenza Virus 3.

- [63123] VGAM1913 precursor RNA folds onto itself, forming VGAM1913 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [63124] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1913 folded precursor RNA into VGAM1913 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM1913 RNA is designated SEQ ID:4624, and is provided hereinbelow with reference to the sequence listing part.

[63125] VGAM1913 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1913 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1913 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63126] VGAM1913 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1913 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1913 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1913 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1913 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63127] The complementary binding of VGAM1913 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1913 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1913 host target RNA into VGAM1913 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63128] It is appreciated that VGAM1913 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1913 host target genes. The mRNA of each one of this plurality of VGAM1913 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1913 RNA, herein designated VGAM RNA, and which when bound by VGAM1913 RNA causes



inhibition of translation of respective one or more VGAM1913 host target proteins.

[63129] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1913 gene, herein designated VGAM GENE, on one or more VGAM1913 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63130] It is yet further appreciated that a function of VGAM1913 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1913 include diagnosis, prevention and

treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGAM1913 correlate with, and may be deduced from, the identity of the host target genes which VGAM1913 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63131] Nucleotide sequences of the VGAM1913 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1913 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1913 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1913 are further described hereinbelow with reference to Table 1.

[63132] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1913 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1913 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63133] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1913 gene, herein designated VGAM is inhibition of expression of VGAM1913 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1913 correlate with, and may be deduced from, the identity of the target genes which VGAM1913 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63134] Mesenchyme Homeo Box 2 (growth arrest-specific homeo box) (MEOX2, Accession NM\_005924) is a VGAM1913 host target gene. MEOX2 BINDING SITE1 and MEOX2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MEOX2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEOX2 BINDING SITE1 and MEOX2 BINDING SITE2, designated SEQ ID:12549 and SEQ ID:12550 respectively, to the nucleotide sequence of VGAM1913 RNA, herein designated VGAM RNA, also designated SEQ ID:4624.

[63135] A function of VGAM1913 is therefore inhibition of Mesenchyme Homeo Box 2 (growth arrest-specific homeo box) (MEOX2, Accession NM\_005924), a gene which roles in mesoderm induction and, somitogenesis, and myogenic and sclerotomal differentiation. Accordingly, utilities of VGAM1913 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MEOX2. The function of MEOX2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827. KIAA0971 (Accession NM\_014929) is another VGAM1913 host target gene. KIAA0971 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0971 BINDING SITE, designated SEQ ID:17224, to the nucleotide sequence of VGAM1913 RNA, herein designated VGAM RNA, also designated SEQ ID:4624.

[63136] Another function of VGAM1913 is therefore inhibition of KIAA0971 (Accession NM\_014929). Accordingly, utilities of VGAM1913 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0971. LOC158435 (Accession NM\_138497) is another VGAM1913 host target gene. LOC158435 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158435, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158435 BINDING SITE, designated SEQ ID:28845, to the nucleotide sequence of VGAM1913 RNA, herein designated VGAM RNA, also designated SEQ ID:4624.

[63137] Another function of VGAM1913 is therefore inhibition of LOC158435 (Accession NM\_138497). Accordingly, utilities of VGAM1913 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158435. LOC220827 (Accession XM\_166052) is another VGAM1913 host target gene. LOC220827 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220827 BINDING SITE, designated SEQ ID:43843, to the nucleotide sequence of VGAM1913 RNA, herein designated VGAM RNA, also designated SEQ ID:4624.

[63138] Another function of VGAM1913 is therefore inhibition of LOC220827 (Accession XM\_166052). Accordingly, utilities of VGAM1913 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC220827. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1914 (VGAM1914) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63139] VGAM1914 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1914 was detected is described hereinabove with reference to Figs. 1–8.

[63140] VGAM1914 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 3. VGAM1914 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63141] VGAM1914 gene encodes a VGAM1914 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1914 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1914 precursor RNA is designated SEQ ID:1900, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1900 is located at position 14210 relative to the genome of Human Parainfluenza Virus 3.

- [63142] VGAM1914 precursor RNA folds onto itself, forming VGAM1914 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [63143] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1914 folded precursor RNA into VGAM1914 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1914 RNA is designated SEQ ID:4625, and is provided hereinbelow with reference to the sequence listing part.

[63144] VGAM1914 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1914 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1914 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63145] VGAM1914 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1914 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1914 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1914 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in



untranslated regions of a VGAM1914 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63146] The complementary binding of VGAM1914 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1914 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1914 host target RNA into VGAM1914 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63147] It is appreciated that VGAM1914 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1914 host target genes. The mRNA of each one of this plurality of VGAM1914 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1914 RNA, herein designated VGAM RNA, and which when bound by VGAM1914 RNA causes

inhibition of translation of respective one or more VGAM1914 host target proteins.

[63148] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1914 gene, herein designated VGAM GENE, on one or more VGAM1914 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63149] It is yet further appreciated that a function of VGAM1914 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1914 include diagnosis, prevention and

treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGAM1914 correlate with, and may be deduced from, the identity of the host target genes which VGAM1914 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63150] Nucleotide sequences of the VGAM1914 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1914 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1914 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1914 are further described hereinbelow with reference to Table 1.

[63151] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1914 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1914 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63152] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1914 gene, herein designated VGAM is inhibition of expression of VGAM1914 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1914 correlate with, and may be deduced from, the identity of the target genes which VGAM1914 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63153] Cartilage Associated Protein (CRTAP, Accession NM\_006371) is a VGAM1914 host target gene. CRTAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRTAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRTAP BINDING SITE, designated SEQ ID:13060, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63154] A function of VGAM1914 is therefore inhibition of Cartilage Associated Protein (CRTAP, Accession NM\_006371), a gene which is a novel developmentally regulated chick embryo protein. Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRTAP. The function of CRTAP and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM152. Integrin, Alpha 5 (fibronectin receptor, alpha polypeptide) (ITGA5, Accession XM\_028642) is another VGAM1914 host target gene. ITGA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA5 BINDING SITE, designated SEQ ID:30724, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63155] Another function of VGAM1914 is therefore inhibition of Integrin, Alpha 5 (fibronectin receptor, alpha polypeptide) (ITGA5, Accession XM\_028642), a gene which is receptor for fibronectin and fibrinogen and recognizes the sequence r-g-d in its ligands. Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA5. The function of ITGA5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1220. Leptin (obesity homolog, mouse) (LEP, Ac-

cession NM\_000230) is another VGAM1914 host target gene. LEP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEP BINDING SITE, designated SEQ ID:5739, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63156] Another function of VGAM1914 is therefore inhibition of Leptin (obesity homolog, mouse) (LEP, Accession NM\_000230). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEP. SRY (sex determining region Y)-box 4 (SOX4, Accession NM\_003107) is another VGAM1914 host target gene. SOX4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOX4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX4 BINDING SITE, designated SEQ ID:9076, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4625.

[63157] Another function of VGAM1914 is therefore inhibition of SRY (sex determining region Y)-box 4 (SOX4, Accession NM\_003107), a gene which binds with high affinity to the t-cell enhancer motif 5'-aacaag-3' motif. Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOX4. The function of SOX4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM409. T-cell Leukemia, Homeobox 1 (TLX1, Accession NM\_005521) is another VGAM1914 host target gene. TLX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TLX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLX1 BINDING SITE, designated SEQ ID:12043, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63158] Another function of VGAM1914 is therefore inhibition of T-cell Leukemia, Homeobox 1 (TLX1, Accession

NM\_005521), a gene which controls the spleen development. Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLX1. The function of TLX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1505. TRHDE (Accession NM\_013381) is another VGAM1914 host target gene. TRHDE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRHDE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRHDE BINDING SITE, designated SEQ ID:15033, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63159] Another function of VGAM1914 is therefore inhibition of TRHDE (Accession NM\_013381). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRHDE. ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577) is another VGAM1914 host target gene. ATP9A BINDING



SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31074, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63160] Another function of VGAM1914 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. AUT-like 1, Cysteine Endopeptidase (*S. cerevisiae*) (AUTL1, Accession NM\_032852) is another VGAM1914 host target gene. AUTL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AUTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AUTL1 BINDING SITE, designated SEQ ID:26648, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ

ID:4625.

[63161] Another function of VGAM1914 is therefore inhibition of AUT-like 1, Cysteine Endopeptidase (*S. cerevisiae*) (AUTL1, Accession NM\_032852). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AUTL1. Chromosome 6 Open Reading Frame 33 (C6orf33, Accession NM\_133367) is another VGAM1914 host target gene. C6orf33 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf33 BINDING SITE, designated SEQ ID:28491, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63162] Another function of VGAM1914 is therefore inhibition of Chromosome 6 Open Reading Frame 33 (C6orf33, Accession NM\_133367). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf33. DK-FZP586N0721 (Accession NM\_015400) is another

VGAM1914 host target gene. DKFZP586N0721 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP586N0721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586N0721 BINDING SITE, designated SEQ ID:17709, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63163] Another function of VGAM1914 is therefore inhibition of DKFZP586N0721 (Accession NM\_015400). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586N0721. FLJ10450 (Accession NM\_018095) is another VGAM1914 host target gene. FLJ10450 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10450 BINDING SITE, designated SEQ ID:19862, to the nucleotide sequence of VGAM1914 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4625.

[63164] Another function of VGAM1914 is therefore inhibition of FLJ10450 (Accession NM\_018095). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10450. GDNF Family Receptor Alpha 4 (GFRA4, Accession NM\_022139) is another VGAM1914 host target gene. GFRA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFRA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFRA4 BINDING SITE, designated SEQ ID:22701, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63165] Another function of VGAM1914 is therefore inhibition of GDNF Family Receptor Alpha 4 (GFRA4, Accession NM\_022139). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFRA4. KIAA0599 (Accession XM\_085127) is another VGAM1914 host target gene. KIAA0599 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by KIAA0599, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0599 BINDING SITE, designated SEQ ID:37852, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63166] Another function of VGAM1914 is therefore inhibition of KIAA0599 (Accession XM\_085127). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0599. KIAA0831 (Accession NM\_014924) is another VGAM1914 host target gene. KIAA0831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0831 BINDING SITE, designated SEQ ID:17207, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63167] Another function of VGAM1914 is therefore inhibition of

KIAA0831 (Accession NM\_014924). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0831. KIAA1493 (Accession XM\_034415) is another VGAM1914 host target gene. KIAA1493 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1493 BINDING SITE, designated SEQ ID:32095, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63168] Another function of VGAM1914 is therefore inhibition of KIAA1493 (Accession XM\_034415). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1493. KIAA1598 (Accession NM\_018330) is another VGAM1914 host target gene. KIAA1598 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1598 BINDING SITE, designated SEQ ID:20332, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63169] Another function of VGAM1914 is therefore inhibition of KIAA1598 (Accession NM\_018330). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1598. MacGAP (Accession NM\_033515) is another VGAM1914 host target gene. MacGAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MacGAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MacGAP BINDING SITE, designated SEQ ID:27291, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63170] Another function of VGAM1914 is therefore inhibition of MacGAP (Accession NM\_033515). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MacGAP. PDZ Domain Containing 2 (PDZD2, Accession

XM\_087705) is another VGAM1914 host target gene.

PDZD2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PDZD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDZD2 BINDING SITE, designated SEQ ID:39392, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63171] Another function of VGAM1914 is therefore inhibition of PDZ Domain Containing 2 (PDZD2, Accession XM\_087705). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDZD2. PRO1728 (Accession NM\_018505) is another VGAM1914 host target gene. PRO1728 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO1728, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1728 BINDING SITE, designated SEQ ID:20572, to the nucleotide sequence of VGAM1914



RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63172] Another function of VGAM1914 is therefore inhibition of PRO1728 (Accession NM\_018505). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1728. RAB11B, Member RAS Oncogene Family (RAB11B, Accession XM\_058232) is another VGAM1914 host target gene. RAB11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB11B BINDING SITE, designated SEQ ID:36588, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63173] Another function of VGAM1914 is therefore inhibition of RAB11B, Member RAS Oncogene Family (RAB11B, Accession XM\_058232). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB11B. LOC150271 (Accession XM\_097859) is another VGAM1914 host target

gene. LOC150271 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41173, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63174] Another function of VGAM1914 is therefore inhibition of LOC150271 (Accession XM\_097859). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC152048 (Accession XM\_098158) is another VGAM1914 host target gene. LOC152048 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152048, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152048 BINDING SITE, designated SEQ ID:41428, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63175] Another function of VGAM1914 is therefore inhibition of LOC152048 (Accession XM\_098158). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152048. LOC153883 (Accession XM\_087798) is another VGAM1914 host target gene. LOC153883 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153883, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153883 BINDING SITE, designated SEQ ID:39433, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63176] Another function of VGAM1914 is therefore inhibition of LOC153883 (Accession XM\_087798). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153883. LOC157869 (Accession XM\_088409) is another VGAM1914 host target gene. LOC157869 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157869, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157869 BINDING SITE, designated SEQ ID:39675, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63177] Another function of VGAM1914 is therefore inhibition of LOC157869 (Accession XM\_088409). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157869. LOC196074 (Accession XM\_113647) is another VGAM1914 host target gene. LOC196074 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196074 BINDING SITE, designated SEQ ID:42320, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63178] Another function of VGAM1914 is therefore inhibition of LOC196074 (Accession XM\_113647). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196074. LOC201292 (Accession XM\_113949) is another VGAM1914 host target gene. LOC201292 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201292 BINDING SITE, designated SEQ ID:42561, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63179] Another function of VGAM1914 is therefore inhibition of LOC201292 (Accession XM\_113949). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201292. LOC221763 (Accession XM\_168107) is another VGAM1914 host target gene. LOC221763 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221763 BINDING SITE, designated SEQ ID:45035, to the nucleotide sequence of VGAM1914 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4625.

[63180] Another function of VGAM1914 is therefore inhibition of LOC221763 (Accession XM\_168107). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221763. LOC89231 (Accession XM\_166577) is another VGAM1914 host target gene. LOC89231 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89231 BINDING SITE, designated SEQ ID:44549, to the nucleotide sequence of VGAM1914 RNA, herein designated VGAM RNA, also designated SEQ ID:4625.

[63181] Another function of VGAM1914 is therefore inhibition of LOC89231 (Accession XM\_166577). Accordingly, utilities of VGAM1914 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89231. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1915 (VGAM1915) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63182] VGAM1915 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1915 was detected is described hereinabove with reference to Figs. 1–8.

[63183] VGAM1915 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 3. VGAM1915 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63184] VGAM1915 gene encodes a VGAM1915 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1915 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1915 precursor RNA is designated SEQ ID:1901, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1901 is located at position 225 relative to the genome of Human Parainfluenza Virus 3.

[63185] VGAM1915 precursor RNA folds onto itself, forming

VGAM1915 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63186] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1915 folded precursor RNA into VGAM1915 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1915 RNA is designated SEQ ID:4626, and is provided hereinbelow with reference to the sequence listing part.

[63187] VGAM1915 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1915 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1915 host target RNA



comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63188] VGAM1915 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1915 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1915 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1915 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1915 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63189] The complementary binding of VGAM1915 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1915 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1915 host target RNA into VGAM1915 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63190] It is appreciated that VGAM1915 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1915 host target genes. The mRNA of each one of this plurality of VGAM1915 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1915 RNA, herein designated VGAM RNA, and which when bound by VGAM1915 RNA causes inhibition of translation of respective one or more VGAM1915 host target proteins.

[63191] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1915 gene, herein designated VGAM GENE, on one or more VGAM1915 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63192] It is yet further appreciated that a function of VGAM1915 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGAM1915 correlate with, and may be deduced from, the identity of the host target genes which VGAM1915 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63193] Nucleotide sequences of the VGAM1915 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1915 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1915 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1915 are further described hereinbelow with reference to Table 1.

[63194] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1915 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1915 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63195] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1915 gene, herein designated VGAM is inhibition of expression of VGAM1915 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1915 correlate with, and may be deduced from, the identity of the target genes which VGAM1915 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63196] Adenosine Deaminase, RNA-specific, B1 (RED1 homolog rat) (ADARB1, Accession NM\_015833) is a VGAM1915 host target gene. ADARB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADARB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADARB1 BINDING SITE,

designated SEQ ID:17949, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63197] A function of VGAM1915 is therefore inhibition of Adenosine Deaminase, RNA-specific, B1 (RED1 homolog rat) (ADARB1, Accession NM\_015833), a gene which RNA editing involves the deamination of adenosines at specific sites. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADARB1. The function of ADARB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1717.B29 (Accession NM\_031939) is another VGAM1915 host target gene. B29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B29 BINDING SITE, designated SEQ ID:25683, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63198] Another function of VGAM1915 is therefore inhibition of

B29 (Accession NM\_031939). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B29. B-cell CLL/lymphoma 11B (zinc finger protein) (BCL11B, Accession NM\_022898) is another VGAM1915 host target gene. BCL11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL11B BINDING SITE, designated SEQ ID:23172, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63199] Another function of VGAM1915 is therefore inhibition of B-cell CLL/lymphoma 11B (zinc finger protein) (BCL11B, Accession NM\_022898). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL11B. Calumenin (CALU, Accession NM\_001219) is another VGAM1915 host target gene. CALU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALU, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALU BINDING SITE, designated SEQ ID:6883, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63200] Another function of VGAM1915 is therefore inhibition of Calumenin (CALU, Accession NM\_001219), a gene which binds 7 calcium ions with a low affinity with unidentified function. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALU. The function of CALU and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM253.Cytoplasmic Linker Associated Protein 2 (CLASP2, Accession XM\_035453) is another VGAM1915 host target gene. CLASP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLASP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLASP2 BINDING SITE, des-



ignated SEQ ID:32267, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63201] Another function of VGAM1915 is therefore inhibition of Cytoplasmic Linker Associated Protein 2 (CLASP2, Accession XM\_035453), a gene which is involved in the regional regulation of microtubule dynamics in motile fibroblasts. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLASP2. The function of CLASP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM897. DUTP Pyrophosphatase (DUT, Accession NM\_001948) is another VGAM1915 host target gene. DUT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DUT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUT BINDING SITE, designated SEQ ID:7663, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63202] Another function of VGAM1915 is therefore inhibition of DUTP Pyrophosphatase (DUT, Accession NM\_001948), a gene which is involved in nucleotide metabolism. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DUT. The function of DUT has been established by previous studies. Deoxyuridine triphosphate nucleotidohydrolase (dUTPase; EC 3.6.1.23) hydrolyzes dUTP to dUMP and pyrophosphate. Mutations in dUTPase of *E. coli* lead to increased dUTP levels and unusually high levels of dUMP incorporation into DNA during replication and repair which, in turn, causes DNA fragmentation and cell death (Lindahl, 1982; el-Hajj et al., 1988). Presumably for this reason, null mutants of dUTPase in yeast are lethal. A second function for dUTPase is to provide dUMP for synthesis of thymidylate. Canman et al. (1992, 1994) showed that increased dUTPase levels in some cancer cell lines accounted for their resistance to the thymidine synthase inhibitor fluorodeoxyuridine (FUdR). McIntosh et al. (1992) cloned 2 functional human dUTP pyrophosphatases from a cDNA expression library by genetic complementation in *E. coli*. The 2 different-sized cDNAs each contain a single long ORF encoding a 141-amino acid polypeptide with a

calculated molecular mass of 16.6 kD. The human protein shares 35% homology with the *E. coli* dUTPase and 53% with the *Saccharomyces cerevisiae* enzyme. McIntosh et al. (1992) detected expression of the dUTPase gene in a variety of human tissues. Because of its possible essential role in DNA replication, the authors suggested that chemotherapeutics could be designed to target dUTPase in human cancers.

[63203] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63204] Canman, C. E.; Radany, E. H.; Parsels, L. A.; Davis, M. A.; Lawrence, T. S.; Maybaum, J. : Induction of resistance to fluorodeoxyuridine cytotoxicity and DNA damage in human tumor cells by expression of *Escherichia coli* deoxyuridinetriphosphatase. *Cancer Res.* 54: 2296–2298, 1994. ; and

[63205] McIntosh, E. M.; Ager, D. D.; Gadsden, M. H.; Haynes, R. H. : Human dUTP pyrophosphatase: cDNA sequence and potential biological importance of the enzyme. *Proc. Nat. Acad. Sci.* 89: 8020.

[63206] Further studies establishing the function and utilities of DUT are found in John Hopkins OMIM database record ID

601266, and in cited publications numbered 9256–9264 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Gardner–Rasheed Feline Sarcoma Viral (v-fgr) Oncogene Homolog (FGR, Accession NM\_005248) is another VGAM1915 host target gene. FGR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGR BINDING SITE, designated SEQ ID:11757, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63207] Another function of VGAM1915 is therefore inhibition of Gardner–Rasheed Feline Sarcoma Viral (v-fgr) Oncogene Homolog (FGR, Accession NM\_005248), a gene which Member of the tyrosine kinase family. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGR. The function of FGR has been established by previous studies. The cell-derived domain of Gardner–Rasheed feline sarcoma virus consists of a gamma-actin sequence and a tyrosine-specific protein kinase sequence

called v-fgr. By means of a v-fgr probe, Tronick et al. (1985) isolated a human homolog. Analysis showed that the human DNA is distinct from all other retroviral oncogenes. They localized the FGR oncogene to 1p36.2-p36.1 by in situ hybridization. By Southern analysis of somatic cell hybrids, Nishizawa et al. (1986) confirmed the assignment of the FGR locus to chromosome 1. FGR, which is the presently used designation, is the same as the oncogene earlier called SRC2. The latter was mapped to 1p36-p34 by Le Beau et al. (1984) using in situ hybridization and by Lebo et al. (1984) using dual-beam chromosome sorting and spot blot DNA analysis. Dracopoli et al. (1988) assigned SRC2 to 1p by analysis of DNA from a panel of somatic cell hybrids and by linkage analysis in the CEPH families. The latter studies showed that the SRC2 locus is 3.1 cM from the Rh blood group locus. They favored the gene order:

1pter--PND--ALPL--FUCA1--SRC2(FGR)--Rh--D1S57--MYCL.

[63208] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63209] Dracopoli, N. C.; Stanger, B. Z.; Lager, M.; Housman, D. E.

: Localization of the FGR protooncogene on the genetic linkage map of human chromosome 1p. Genomics 3: 124–128, 1988. ; and

[63210] Nishizawa, M.; Semba, K.; Yoshida, M. C.; Yamamoto, T.; Sasaki, M.; Toyoshima, K. : Structure, expression, and chromosomal location of the human c-fgr gene. Molec. Cell. Biol. 6: 511–517.

[63211] Further studies establishing the function and utilities of FGR are found in John Hopkins OMIM database record ID 164940, and in cited publications numbered 10881–1088 and 10801–10802 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myeloperoxidase (MPO, Accession NM\_000250) is another VGAM1915 host target gene. MPO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPO BINDING SITE, designated SEQ ID:5787, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63212] Another function of VGAM1915 is therefore inhibition of

Myeloperoxidase (MPO, Accession NM\_000250), a gene which is present in primary granules of neutrophilic granulocytes. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPO. The function of MPO has been established by previous studies. Weil et al. (1988) found that the MPO gene was translocated to chromosome 15 in all cases of acute promyelocytic leukemia (subtype M3), which is consistently associated with the chromosomal translocation  $t(15;17)(q22;q11.2)$ . In 2 of 4 cases examined by genomic blot analysis, rearrangement of the MPO gene was detected in leukemia cells. Weil et al. (1988) also suggested that MPO may be pivotal in the pathogenesis of APL. According to HGM10, the MPO gene is located at a distance from the breakpoint in APL, and the gene itself is probably usually not rearranged in APL. Myeloperoxidase has been detected in activated microglial macrophages and within amyloid plaques in the central nervous system. Using statistical analysis, Reynolds et al. (2000) examined the relationship between APOE (OMIM Ref. No. 107741) and MPO polymorphisms in the risk of Alzheimer disease (AD; 104300) in a genetically homogeneous Finnish population. They found that the presence of

the MPO A allele in conjunction with APOE E4 significantly increased the risk of AD in men, but not in women (odds ratio for men with both alleles = 11.4 vs APOE E4 alone = 3.0). Reynolds et al. (2000) also found that estrogen receptor- $\alpha$  (OMIM Ref. No. 133430) binds to the MPO A promoter, which may explain the gender differences.

[63213] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63214] Reynolds, W. F.; Hiltunen, M.; Pirskanen, M.; Mannermaa, A.; Helisalmi, S.; Lehtovirta, M.; Alafuzoff, I.; Soininen, H. : MPO and APOE epsilon-4 polymorphisms interact to increase risk for AD in Finnish males. *Neurology* 55: 1284-1290, 2000. ; and

[63215] Weil, S. C.; Rosner, G. L.; Reid, M. S.; Chisholm, R. L.; Lemons, R. S.; Swanson, M. S.; Carrino, J. J.; Diaz, M. O.; Le Beau, M. M. : Translocation and rearrangement of myeloperoxidase.

[63216] Further studies establishing the function and utilities of MPO are found in John Hopkins OMIM database record ID 606989, and in cited publications numbered 5531-5541, 5569, 6146-615 and 9098-6160 listed in the bibliography section hereinbelow, which are also hereby incorpo-



rated by reference. Myotubularin Related Protein 8 (MTMR8, Accession NM\_015458) is another VGAM1915 host target gene. MTMR8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTMR8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR8 BINDING SITE, designated SEQ ID:17750, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63217] Another function of VGAM1915 is therefore inhibition of Myotubularin Related Protein 8 (MTMR8, Accession NM\_015458), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTMR8. The function of MTMR8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM379. Nuclear Factor Related to Kappa B Binding Protein (NFRKB, Accession NM\_006165) is another VGAM1915 host target gene. NFRKB BINDING SITE is HOST

TARGET binding site found in the 5' untranslated region of mRNA encoded by NFRKB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFRKB BINDING SITE, designated SEQ ID:12821, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63218] Another function of VGAM1915 is therefore inhibition of Nuclear Factor Related to Kappa B Binding Protein (NFRKB, Accession NM\_006165). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFRKB. 2'-5'-oligoadenylate Synthetase 2, 69/71kDa (OAS2, Accession NM\_016817) is another VGAM1915 host target gene. OAS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAS2 BINDING SITE, designated SEQ ID:18805, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63219] Another function of VGAM1915 is therefore inhibition of 2'-5'-oligoadenylate Synthetase 2, 69/71kDa (OAS2, Accession NM\_016817), a gene which may play a role in mediating resistance to virus infection, control of cell growth, differentiation, and apoptosis. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAS2. The function of OAS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1498. Proteasome (prosome, macropain) Subunit, Beta Type, 9 (large multifunctional protease 2) (PSMB9, Accession NM\_002800) is another VGAM1915 host target gene. PSMB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMB9 BINDING SITE, designated SEQ ID:8675, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63220] Another function of VGAM1915 is therefore inhibition of

Proteasome (prosome, macropain) Subunit, Beta Type, 9 (large multifunctional protease 2) (PSMB9, Accession NM\_002800), a gene which is one component of a multicatalytic proteinase complex. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMB9. The function of PSMB9 has been established by previous studies. Driscoll et al. (1993) showed that the MHC-linked LMP2 and LMP7 subunits function to amplify specific endopeptidase activities of the proteasome. Gaczynska et al. (1993) presented experiments suggesting that gamma-interferon and expression of the LMP2 and LMP7 genes should favor the production by proteasomes of the types of peptides found on MHC class I molecules, which terminate almost exclusively with hydrophobic or basic residues. Animal model experiments lend further support to the function of PSMB9. Van Kaer et al. (1994) generated healthy mice with disrupted *Lmp2* genes. Proteasomal peptidase activity against hydrophobic and basic substrates but not acidic substrates was lower in spleen and liver from mutant mice compared with wildtype mice. Differences in muscle and brain were not significant. Although flow cytometric analysis showed no difference in

MHC class I expression, antigen-presenting cells from mutant mice were less able to stimulate a T-cell hybridoma specific for a nucleoprotein (NP) envelope antigen of an influenza A virus. Mutant mice also had less than half of the wildtype levels of CD8 (see OMIM Ref. No. 186910)-positive T lymphocytes and generated much lower levels of cytotoxic T-cell precursors specific for NP, though not for ovalbumin. Van Kaer et al. (1994) concluded that LMP2 selectively influences antigen processing of MHC class I-restricted antigens.

[63221] It is appreciated that the abovementioned animal model for PSMB9 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[63222] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63223] Van Kaer, L.; Ashton-Rickardt, P. G.; Eichelberger, M.; Gaczynska, M.; Nagashima, K.; Rock, K. L.; Goldberg, A. L.; Doherty, P. C.; Tonegawa, S. : Altered peptidase and viral-specific T cell response in LMP2 mutant mice. *Immunity* 1: 533-541, 1994. ; and

[63224] Driscoll, J.; Brown, M. G.; Finley, D.; Monaco, J. J. : MHC-

linked LMP gene products specifically alter peptidase activities of the proteasome. Nature 365: 262–264, 1993.

[63225] Further studies establishing the function and utilities of PSMB9 are found in John Hopkins OMIM database record ID 177045, and in cited publications numbered 1172–1175, 420 and 9736–9740 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_030671) is another VGAM1915 host target gene. PTPRO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPRO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE, designated SEQ ID:25032, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63226] Another function of VGAM1915 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_030671), a gene which may function as a cell contact receptor that mediates and controls cell–cell signals. Accordingly, utilities of VGAM1915 include diag–

nosis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM140. Reticulon 1 (RTN1, Accession NM\_021136) is another VGAM1915 host target gene. RTN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RTN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RTN1 BINDING SITE, designated SEQ ID:22108, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63227] Another function of VGAM1915 is therefore inhibition of Reticulon 1 (RTN1, Accession NM\_021136), a gene which may be involved in neuroendocrine secretion or in membrane – membrane trafficking in neuroendocrine cells. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RTN1. The function of RTN1 and its association with various diseases and clinical conditions, has

been established by previous studies, as described herein above with reference to VGAM337. Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754) is another VGAM1915 host target gene. RUNX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RUNX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RUNX1 BINDING SITE, designated SEQ ID:7494, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63228] Another function of VGAM1915 is therefore inhibition of Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RUNX1. Tetratricopeptide Repeat Domain 3 (TTC3, Accession NM\_003316) is another VGAM1915 host target gene. TTC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TTC3, corresponding to a



HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTC3 BINDING SITE, designated SEQ ID:9318, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63229] Another function of VGAM1915 is therefore inhibition of Tetratricopeptide Repeat Domain 3 (TTC3, Accession NM\_003316), a gene which contains tetratricopeptide repeat (TPR) motifs. Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTC3. The function of TTC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM699.Zic Family Member 3 Heterotaxy 1 (odd-paired homolog, Drosophila) (ZIC3, Accession NM\_003413) is another VGAM1915 host target gene. ZIC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZIC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZIC3 BINDING SITE, desig-

nated SEQ ID:9450, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63230] Another function of VGAM1915 is therefore inhibition of Zic Family Member 3 Heterotaxy 1 (odd-paired homolog, *Drosophila*) (ZIC3, Accession NM\_003413). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZIC3. Chromosome 1 Open Reading Frame 19 (C1orf19, Accession XM\_042962) is another VGAM1915 host target gene. C1orf19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf19 BINDING SITE, designated SEQ ID:33840, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63231] Another function of VGAM1915 is therefore inhibition of Chromosome 1 Open Reading Frame 19 (C1orf19, Accession XM\_042962). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with C1orf19. DKFZP564I0422 (Accession NM\_031435) is another VGAM1915 host target gene. DKFZP564I0422 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564I0422, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564I0422 BINDING SITE, designated SEQ ID:25432, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63232] Another function of VGAM1915 is therefore inhibition of DKFZP564I0422 (Accession NM\_031435). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I0422. FACTP140 (Accession NM\_007192) is another VGAM1915 host target gene. FACTP140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FACTP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FACTP140 BINDING SITE, designated SEQ ID:14047, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63233] Another function of VGAM1915 is therefore inhibition of FACTP140 (Accession NM\_007192). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FACTP140. FLJ12644 (Accession NM\_023074) is another VGAM1915 host target gene. FLJ12644 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12644 BINDING SITE, designated SEQ ID:23330, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63234] Another function of VGAM1915 is therefore inhibition of FLJ12644 (Accession NM\_023074). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12644. FLJ12806 (Accession NM\_022831) is another VGAM1915 host target gene. FLJ12806 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12806, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12806 BINDING SITE, designated SEQ ID:23109, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63235] Another function of VGAM1915 is therefore inhibition of FLJ12806 (Accession NM\_022831). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12806. FLJ22329 (Accession NM\_024656) is another VGAM1915 host target gene. FLJ22329 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22329, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22329 BINDING SITE, designated SEQ ID:23960, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63236] Another function of VGAM1915 is therefore inhibition of

FLJ22329 (Accession NM\_024656). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22329. FLJ23045 (Accession NM\_024704) is another VGAM1915 host target gene. FLJ23045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23045 BINDING SITE, designated SEQ ID:24021, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63237] Another function of VGAM1915 is therefore inhibition of FLJ23045 (Accession NM\_024704). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23045. Glia Maturation Factor, Beta (GMFB, Accession NM\_004124) is another VGAM1915 host target gene. GMFB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GMFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of GMFB BINDING SITE, designated SEQ ID:10329, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63238] Another function of VGAM1915 is therefore inhibition of Glia Maturation Factor, Beta (GMFB, Accession NM\_004124). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMFB. GOLGIN-67 (Accession XM\_170772) is another VGAM1915 host target gene. GOLGIN-67 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLGIN-67, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGIN-67 BINDING SITE, designated SEQ ID:45538, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63239] Another function of VGAM1915 is therefore inhibition of GOLGIN-67 (Accession XM\_170772). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

GOLGIN-67. KIAA0766 (Accession NM\_014805) is another VGAM1915 host target gene. KIAA0766 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0766 BINDING SITE, designated SEQ ID:16741, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63240] Another function of VGAM1915 is therefore inhibition of KIAA0766 (Accession NM\_014805). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0766. KIAA0855 (Accession NM\_015003) is another VGAM1915 host target gene. KIAA0855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0855 BINDING SITE, designated SEQ ID:17379, to the nucleotide sequence of VGAM1915 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4626.

[63241] Another function of VGAM1915 is therefore inhibition of KIAA0855 (Accession NM\_015003). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0855. KIAA0993 (Accession XM\_034413) is another VGAM1915 host target gene. KIAA0993 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0993, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0993 BINDING SITE, designated SEQ ID:32076, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63242] Another function of VGAM1915 is therefore inhibition of KIAA0993 (Accession XM\_034413). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0993. KIAA1323 (Accession XM\_032146) is another VGAM1915 host target gene. KIAA1323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1323, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1323 BINDING SITE, designated SEQ ID:31574, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63243] Another function of VGAM1915 is therefore inhibition of KIAA1323 (Accession XM\_032146). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1323. Peroxisomal Biogenesis Factor 11B (PEX11B, Accession NM\_003846) is another VGAM1915 host target gene. PEX11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEX11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEX11B BINDING SITE, designated SEQ ID:9943, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63244] Another function of VGAM1915 is therefore inhibition of Peroxisomal Biogenesis Factor 11B (PEX11B, Accession

NM\_003846). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEX11B. PRO1992 (Accession NM\_014107) is another VGAM1915 host target gene. PRO1992 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1992 BINDING SITE, designated SEQ ID:15336, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63245] Another function of VGAM1915 is therefore inhibition of PRO1992 (Accession NM\_014107). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1992. RABEX5 (Accession NM\_014504) is another VGAM1915 host target gene. RABEX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RABEX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of RABEX5 BINDING SITE, designated SEQ ID:15841, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63246] Another function of VGAM1915 is therefore inhibition of RABEX5 (Accession NM\_014504). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RABEX5. Retinoblastoma Binding Protein 4 (RBBP4, Accession NM\_005610) is another VGAM1915 host target gene. RBBP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RBBP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBBP4 BINDING SITE, designated SEQ ID:12131, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63247] Another function of VGAM1915 is therefore inhibition of Retinoblastoma Binding Protein 4 (RBBP4, Accession NM\_005610). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with RBBP4. Ring Finger Protein 24 (RNF24, Accession NM\_007219) is another VGAM1915 host target gene. RNF24 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RNF24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF24 BINDING SITE, designated SEQ ID:14085, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63248] Another function of VGAM1915 is therefore inhibition of Ring Finger Protein 24 (RNF24, Accession NM\_007219). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF24. Solute Carrier Family 26, Member 10 (SLC26A10, Accession NM\_133489) is another VGAM1915 host target gene. SLC26A10 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SLC26A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

SLC26A10 BINDING SITE, designated SEQ ID:28558, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63249] Another function of VGAM1915 is therefore inhibition of Solute Carrier Family 26, Member 10 (SLC26A10, Accession NM\_133489). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A10.

Thioesterase, Adipose Associated (THEA, Accession XM\_038922) is another VGAM1915 host target gene.

THEA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by THEA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THEA BINDING SITE, designated SEQ ID:32946, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63250] Another function of VGAM1915 is therefore inhibition of Thioesterase, Adipose Associated (THEA, Accession XM\_038922). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THEA. UPLC1 (Accession

NM\_017707) is another VGAM1915 host target gene.

UPLC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by UPLC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UPLC1 BINDING SITE, designated SEQ ID:19286, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63251] Another function of VGAM1915 is therefore inhibition of UPLC1 (Accession NM\_017707). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UPLC1. LOC145988 (Accession XM\_085290) is another VGAM1915 host target gene. LOC145988 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145988 BINDING SITE, designated SEQ ID:38044, to the nucleotide sequence of VGAM1915 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4626.

[63252] Another function of VGAM1915 is therefore inhibition of LOC145988 (Accession XM\_085290). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145988. LOC146880 (Accession XM\_085627) is another VGAM1915 host target gene. LOC146880 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146880, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146880 BINDING SITE, designated SEQ ID:38257, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63253] Another function of VGAM1915 is therefore inhibition of LOC146880 (Accession XM\_085627). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146880. LOC150519 (Accession XM\_086937) is another VGAM1915 host target gene. LOC150519 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150519, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150519 BINDING SITE, designated SEQ ID:38988, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63254] Another function of VGAM1915 is therefore inhibition of LOC150519 (Accession XM\_086937). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150519. LOC152373 (Accession XM\_087449) is another VGAM1915 host target gene. LOC152373 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152373 BINDING SITE, designated SEQ ID:39269, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63255] Another function of VGAM1915 is therefore inhibition of LOC152373 (Accession XM\_087449). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC152373. LOC158969 (Accession XM\_088728) is another VGAM1915 host target gene. LOC158969 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158969, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158969 BINDING SITE, designated SEQ ID:39917, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63256] Another function of VGAM1915 is therefore inhibition of LOC158969 (Accession XM\_088728). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158969. LOC220980 (Accession XM\_167629) is another VGAM1915 host target gene. LOC220980 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC220980, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220980 BINDING SITE, designated SEQ ID:44742, to

the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63257] Another function of VGAM1915 is therefore inhibition of LOC220980 (Accession XM\_167629). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220980. LOC222999 (Accession XM\_170185) is another VGAM1915 host target gene. LOC222999 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222999, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222999 BINDING SITE, designated SEQ ID:45312, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63258] Another function of VGAM1915 is therefore inhibition of LOC222999 (Accession XM\_170185). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222999. LOC51267 (Accession NM\_016511) is another VGAM1915 host target gene. LOC51267 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC51267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51267 BINDING SITE, designated SEQ ID:18592, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63259] Another function of VGAM1915 is therefore inhibition of LOC51267 (Accession NM\_016511). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51267. LOC90268 (Accession XM\_030424) is another VGAM1915 host target gene. LOC90268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90268 BINDING SITE, designated SEQ ID:31044, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63260] Another function of VGAM1915 is therefore inhibition of LOC90268 (Accession XM\_030424). Accordingly, utilities

of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90268. LOC91145 (Accession XM\_036454) is another VGAM1915 host target gene. LOC91145 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91145, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91145 BINDING SITE, designated SEQ ID:32449, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63261] Another function of VGAM1915 is therefore inhibition of LOC91145 (Accession XM\_036454). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91145. LOC91963 (Accession XM\_041902) is another VGAM1915 host target gene. LOC91963 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91963, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC91963 BINDING SITE, designated SEQ ID:33627, to the nucleotide sequence of VGAM1915 RNA, herein designated VGAM RNA, also designated SEQ ID:4626.

[63262] Another function of VGAM1915 is therefore inhibition of LOC91963 (Accession XM\_041902). Accordingly, utilities of VGAM1915 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91963. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1916 (VGAM1916) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63263] VGAM1916 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1916 was detected is described hereinabove with reference to Figs. 1–8.

[63264] VGAM1916 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 1 Strain Washington/1964. VGAM1916 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63265] VGAM1916 gene encodes a VGAM1916 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1916 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1916 precursor RNA is designated SEQ ID:1902, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1902 is located at position 4687 relative to the genome of Human Parainfluenza Virus 1 Strain Washington/1964.

[63266] VGAM1916 precursor RNA folds onto itself, forming VGAM1916 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63267] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1916 folded precursor RNA into VGAM1916 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1916 RNA is designated SEQ ID:4627, and is provided hereinbelow with reference to the sequence listing part.

[63268] VGAM1916 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1916 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1916 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63269] VGAM1916 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1916 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1916 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-



quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1916 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1916 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63270] The complementary binding of VGAM1916 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1916 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1916 host target RNA into VGAM1916 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63271] It is appreciated that VGAM1916 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1916 host target genes. The mRNA of each one of this plurality of VGAM1916 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1916 RNA, herein designated VGAM RNA, and which when bound by VGAM1916 RNA causes inhibition of translation of respective one or more VGAM1916 host target proteins.

[63272] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1916 gene, herein designated VGAM GENE, on one or more VGAM1916 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63273] It is yet further appreciated that a function of VGAM1916 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1916 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 1 Strain Washington/1964. Specific functions, and accordingly utilities, of VGAM1916 correlate with, and may be deduced from, the identity of the host target genes which VGAM1916 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63274] Nucleotide sequences of the VGAM1916 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1916 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1916 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1916 are further described hereinbelow with reference to Table 1.

[63275] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1916 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1916 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63276] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1916 gene, herein designated VGAM is inhibition of expression of VGAM1916 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1916 correlate with, and may be deduced from, the identity of the target genes which VGAM1916 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63277] AAT1 (Accession XM\_087415) is a VGAM1916 host target gene. AAT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AAT1 BINDING SITE, designated SEQ ID:39227, to the nucleotide sequence of VGAM1916 RNA, herein designated VGAM RNA, also designated SEQ ID:4627.

[63278] A function of VGAM1916 is therefore inhibition of AAT1

(Accession XM\_087415), a gene which linkage between A1BG and Lutheran blood group . Accordingly, utilities of VGAM1916 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AAT1. The function of AAT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM357. Angiotensin Like 1 (AMOTL1, Accession XM\_057045) is another VGAM1916 host target gene. AMOTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMOTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOTL1 BINDING SITE, designated SEQ ID:36462, to the nucleotide sequence of VGAM1916 RNA, herein designated VGAM RNA, also designated SEQ ID:4627.

[63279] Another function of VGAM1916 is therefore inhibition of Angiotensin Like 1 (AMOTL1, Accession XM\_057045). Accordingly, utilities of VGAM1916 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOTL1. DKFZP564C196 (Accession

XM\_046405) is another VGAM1916 host target gene. DKFZP564C196 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564C196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564C196 BINDING SITE, designated SEQ ID:34711, to the nucleotide sequence of VGAM1916 RNA, herein designated VGAM RNA, also designated SEQ ID:4627.

[63280] Another function of VGAM1916 is therefore inhibition of DKFZP564C196 (Accession XM\_046405). Accordingly, utilities of VGAM1916 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564C196. EST-YD1 (Accession NM\_021208) is another VGAM1916 host target gene. EST-YD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EST-YD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EST-YD1 BINDING SITE, designated SEQ ID:22186, to the nucleotide sequence of VGAM1916 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4627.

[63281] Another function of VGAM1916 is therefore inhibition of EST-YD1 (Accession NM\_021208). Accordingly, utilities of VGAM1916 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EST-YD1. MGC4832 (Accession NM\_145061) is another VGAM1916 host target gene. MGC4832 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC4832, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4832 BINDING SITE, designated SEQ ID:29699, to the nucleotide sequence of VGAM1916 RNA, herein designated VGAM RNA, also designated SEQ ID:4627.

[63282] Another function of VGAM1916 is therefore inhibition of MGC4832 (Accession NM\_145061). Accordingly, utilities of VGAM1916 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4832. SH3-domain Kinase Binding Protein 1 (SH3KBP1, Accession XM\_039010) is another VGAM1916 host target gene. SH3KBP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA

encoded by SH3KBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3KBP1 BINDING SITE, designated SEQ ID:32981, to the nucleotide sequence of VGAM1916 RNA, herein designated VGAM RNA, also designated SEQ ID:4627.

[63283] Another function of VGAM1916 is therefore inhibition of SH3-domain Kinase Binding Protein 1 (SH3KBP1, Accession XM\_039010). Accordingly, utilities of VGAM1916 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3KBP1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1917 (VGAM1917) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63284] VGAM1917 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1917 was detected is described hereinabove with reference to Figs. 1-8.

[63285] VGAM1917 gene, herein designated VGAM GENE, is a viral



gene contained in the genome of Human Parainfluenza Virus 1 Strain Washington/1964. VGAM1917 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63286] VGAM1917 gene encodes a VGAM1917 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1917 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1917 precursor RNA is designated SEQ ID:1903, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1903 is located at position 14949 relative to the genome of Human Parainfluenza Virus 1 Strain Washington/1964.

[63287] VGAM1917 precursor RNA folds onto itself, forming VGAM1917 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[63288] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1917 folded precursor RNA into VGAM1917 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 63%) nucleotide sequence of VGAM1917 RNA is designated SEQ ID:4628, and is provided hereinbelow with reference to the sequence listing part.

[63289] VGAM1917 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1917 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1917 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63290] VGAM1917 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1917 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1917 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1917 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1917 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[63291] The complementary binding of VGAM1917 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1917 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1917 host target RNA into VGAM1917 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63292] It is appreciated that VGAM1917 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1917 host target genes. The mRNA of each one of this plurality of VGAM1917 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1917 RNA, herein designated VGAM RNA, and which when bound by VGAM1917 RNA causes inhibition of translation of respective one or more VGAM1917 host target proteins.

[63293] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1917 gene, herein designated VGAM GENE, on one or more VGAM1917 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63294] It is yet further appreciated that a function of VGAM1917 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1917 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 1 Strain Washington/1964. Specific functions, and accordingly utilities, of VGAM1917 correlate with, and may be deduced from, the identity of the host target genes which VGAM1917 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63295] Nucleotide sequences of the VGAM1917 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1917 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1917 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1917 are further described hereinbelow with reference to Table 1.

[63296] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1917 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1917 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63297] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1917 gene, herein designated VGAM is inhibition of expression of VGAM1917 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1917 correlate with, and may be deduced from, the identity of the target genes which VGAM1917 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63298] Adrenergic, Beta-3-, Receptor (ADRB3, Accession NM\_000025) is a VGAM1917 host target gene. ADRB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADRB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of ADRB3 BINDING SITE, designated SEQ ID:5458, to the nucleotide sequence of VGAM1917 RNA, herein designated VGAM RNA, also designated SEQ ID:4628.

[63299] A function of VGAM1917 is therefore inhibition of Adren-  
ergic, Beta-3-, Receptor (ADRB3, Accession NM\_000025),  
a gene which stimulates adenylyl cyclase activity and reg-  
ulates lipolysis. Accordingly, utilities of VGAM1917 in-  
clude diagnosis, prevention and treatment of diseases and  
clinical conditions associated with ADRB3. The function of  
ADRB3 and its association with various diseases and clini-  
cal conditions, has been established by previous studies,  
as described hereinabove with reference to  
VGAM179.Fukuyama Type Congenital Muscular Dystrophy  
(fukutin) (FCMD, Accession NM\_006731) is another  
VGAM1917 host target gene. FCMD BINDING SITE is HOST  
TARGET binding site found in the 3' untranslated region  
of mRNA encoded by FCMD, corresponding to a HOST  
TARGET binding site such as BINDING SITE I, BINDING SITE  
II or BINDING SITE III. Table 2 illustrates the complemen-  
tarity of the nucleotide sequences of FCMD BINDING SITE,  
designated SEQ ID:13570, to the nucleotide sequence of  
VGAM1917 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4628.

[63300] Another function of VGAM1917 is therefore inhibition of Fukuyama Type Congenital Muscular Dystrophy (fukutin) (FCMD, Accession NM\_006731). Accordingly, utilities of VGAM1917 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FCMD. Kallikrein 3, (prostate specific antigen) (KLK3, Accession NM\_001648) is another VGAM1917 host target gene. KLK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLK3 BINDING SITE, designated SEQ ID:7350, to the nucleotide sequence of VGAM1917 RNA, herein designated VGAM RNA, also designated SEQ ID:4628.

[63301] Another function of VGAM1917 is therefore inhibition of Kallikrein 3, (prostate specific antigen) (KLK3, Accession NM\_001648), a gene which functions in the liquefaction of seminal coagulum. Accordingly, utilities of VGAM1917 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLK3. The function of KLK3 has been established by previous studies. Human



prostate-specific antigen (APS) is a kallikrein-like protease present in seminal plasma. It is a single-chain glycoprotein with a molecular mass of about 33 kD which may function normally in the liquefaction of seminal coagulum. Radioimmunoassay of serum levels of this antigen (called PSA in the clinical setting) is useful in the diagnosis and monitoring of prostatic carcinoma (Stamey et al., 1987; Oesterling et al., 1988). (Because PSA is the symbol for the protein S alpha gene (OMIM Ref. No. 176880), APS is used as the gene symbol.) Lundwall and Lilja (1987) cloned a cDNA corresponding to APS, and Schulz et al. (1988) reported the complete sequence of a cDNA encompassing the immature human prostate-specific antigen and an unspliced leader sequence Bansal et al. (2000) investigated the interrelationships of age, PSA, and various zonal measurements in the prostate, and assessed the impact of heritable influences on total PSA. Eighty-four monozygotic twin pairs and 83 dizygotic twin pairs were studied, and serum total PSA, free PSA, and PSA-alpha-1-antichymotrypsin were measured. Their prostate volumes (total (TV), transition zone (TZ), and peripheral zone) were quantitated using transrectal ultrasound. Total PSA was significantly correlated with all zonal

prostate measurements (TZ, peripheral zone, TV, and TZ/TV) and with age. When linear regression was applied, only age and TZ were retained in the final model. The proportion of variability in total PSA explained by these 2 factors, however, was below 24%. In contrast, estimates of heritability showed that approximately 45% of the variability in total PSA could be explained by inherited factors.

[63302] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63303] Bansal, A.; Murray, D. K.; Wu, J. T.; Stephenson, R. A.; Middleton, R. G.; Meikle, A. W. : Heritability of prostate-specific antigen and relationship with zonal prostate volumes in aging twins. J. Clin. Endocr. Metab. 85: 1272–1276, 2000. ; and

[63304] Sutherland, G. R.; Baker, E.; Hyland, V. J.; Callen, D. F.; Close, J. A.; Tregear, G. W.; Evans, B. A.; Richards, R. I. : Human prostate-specific antigen (APS) is a member of the gland.

[63305] Further studies establishing the function and utilities of KLK3 are found in John Hopkins OMIM database record ID 176820, and in cited publications numbered 1639–1640, 11095–11098, 10080–10081, 508 and 4159 listed in the

bibliography section hereinbelow, which are also hereby incorporated by reference. LIM Domain Containing Preferred Translocation Partner In Lipoma (LPP, Accession NM\_005578) is another VGAM1917 host target gene. LPP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPP BINDING SITE, designated SEQ ID:12105, to the nucleotide sequence of VGAM1917 RNA, herein designated VGAM RNA, also designated SEQ ID:4628.

[63306] Another function of VGAM1917 is therefore inhibition of LIM Domain Containing Preferred Translocation Partner In Lipoma (LPP, Accession NM\_005578). Accordingly, utilities of VGAM1917 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPP. RAB11A, Member RAS Oncogene Family (RAB11A, Accession NM\_004663) is another VGAM1917 host target gene. RAB11A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of RAB11A BINDING SITE, designated SEQ ID:11035, to the nucleotide sequence of VGAM1917 RNA, herein designated VGAM RNA, also designated SEQ ID:4628.

[63307] Another function of VGAM1917 is therefore inhibition of RAB11A, Member RAS Oncogene Family (RAB11A, Accession NM\_004663). Accordingly, utilities of VGAM1917 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB11A. HCC-4 (Accession NM\_138611) is another VGAM1917 host target gene. HCC-4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCC-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCC-4 BINDING SITE, designated SEQ ID:28899, to the nucleotide sequence of VGAM1917 RNA, herein designated VGAM RNA, also designated SEQ ID:4628.

[63308] Another function of VGAM1917 is therefore inhibition of HCC-4 (Accession NM\_138611). Accordingly, utilities of VGAM1917 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with HCC-4. IBTK (Accession XM\_041401) is another VGAM1917 host target gene. IBTK BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by IBTK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IBTK BINDING SITE, designated SEQ ID:33517, to the nucleotide sequence of VGAM1917 RNA, herein designated VGAM RNA, also designated SEQ ID:4628.

[63309] Another function of VGAM1917 is therefore inhibition of IBTK (Accession XM\_041401). Accordingly, utilities of VGAM1917 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IBTK. KIAA1641 (Accession XM\_087167) is another VGAM1917 host target gene. KIAA1641 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1641, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1641 BINDING SITE, designated SEQ ID:39099, to the nucleotide sequence of

VGAM1917 RNA, herein designated VGAM RNA, also designated SEQ ID:4628.

[63310] Another function of VGAM1917 is therefore inhibition of KIAA1641 (Accession XM\_087167). Accordingly, utilities of VGAM1917 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1641. LOC220846 (Accession XM\_165515) is another VGAM1917 host target gene. LOC220846 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220846, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220846 BINDING SITE, designated SEQ ID:43660, to the nucleotide sequence of VGAM1917 RNA, herein designated VGAM RNA, also designated SEQ ID:4628.

[63311] Another function of VGAM1917 is therefore inhibition of LOC220846 (Accession XM\_165515). Accordingly, utilities of VGAM1917 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220846. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1918 (VGAM1918) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63312] VGAM1918 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1918 was detected is described hereinabove with reference to Figs. 1–8.

[63313] VGAM1918 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Parainfluenza Virus 1 Strain Washington/1964. VGAM1918 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63314] VGAM1918 gene encodes a VGAM1918 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1918 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1918 precursor RNA is designated SEQ ID:1904, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1904 is located at position 7051 relative to the genome of Human Parainfluenza Virus 1 Strain Washing–

ton/1964.

- [63315] VGAM1918 precursor RNA folds onto itself, forming VGAM1918 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [63316] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1918 folded precursor RNA into VGAM1918 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1918 RNA is designated SEQ ID:4629, and is provided hereinbelow with reference to the sequence listing part.
- [63317] VGAM1918 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1918 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1918 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63318] VGAM1918 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1918 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1918 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1918 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1918 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63319] The complementary binding of VGAM1918 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1918 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1918 host target RNA into VGAM1918 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63320] It is appreciated that VGAM1918 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1918 host target genes. The mRNA of each one of this plurality of VGAM1918 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1918 RNA, herein designated VGAM RNA, and which when bound by VGAM1918 RNA causes inhibition of translation of respective one or more VGAM1918 host target proteins.

[63321] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1918 gene, herein designated VGAM GENE, on one or more VGAM1918 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63322] It is yet further appreciated that a function of VGAM1918 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1918 include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 1 Strain Washington/1964. Specific functions, and accord-

ingly utilities, of VGAM1918 correlate with, and may be deduced from, the identity of the host target genes which VGAM1918 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63323] Nucleotide sequences of the VGAM1918 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1918 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1918 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1918 are further described hereinbelow with reference to Table 1.

[63324] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1918 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1918 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63325] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1918 gene, herein designated VGAM is inhibition of expression of VGAM1918 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1918 correlate with, and may be deduced

from, the identity of the target genes which VGAM1918 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63326] KIAA1036 (Accession NM\_014909) is a VGAM1918 host target gene. KIAA1036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1036 BINDING SITE, designated SEQ ID:17124, to the nucleotide sequence of VGAM1918 RNA, herein designated VGAM RNA, also designated SEQ ID:4629.

[63327] A function of VGAM1918 is therefore inhibition of KIAA1036 (Accession NM\_014909). Accordingly, utilities of VGAM1918 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1036. LOC146713 (Accession XM\_097071) is another VGAM1918 host target gene. LOC146713 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC146713 BINDING SITE, designated SEQ ID:40716, to the nucleotide sequence of VGAM1918 RNA, herein designated VGAM RNA, also designated SEQ ID:4629.

[63328] Another function of VGAM1918 is therefore inhibition of LOC146713 (Accession XM\_097071). Accordingly, utilities of VGAM1918 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146713. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1919 (VGAM1919) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63329] VGAM1919 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1919 was detected is described hereinabove with reference to Figs. 1–8.

[63330] VGAM1919 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1919 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[63331] VGAM1919 gene encodes a VGAM1919 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1919 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1919 precursor RNA is designated SEQ ID:1905, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1905 is located at position 109925 relative to the genome of Equine Herpesvirus 1.

[63332] VGAM1919 precursor RNA folds onto itself, forming VGAM1919 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63333] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1919 folded precursor RNA into VGAM1919 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1919 RNA is designated SEQ ID:4630, and is provided hereinbelow with reference to the sequence listing part.

[63334] VGAM1919 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1919 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1919 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63335] VGAM1919 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1919 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1919 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-



quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1919 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1919 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63336] The complementary binding of VGAM1919 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1919 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1919 host target RNA into VGAM1919 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63337] It is appreciated that VGAM1919 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1919 host target genes. The mRNA of each one of this plurality of VGAM1919 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1919 RNA, herein designated VGAM RNA, and which when bound by VGAM1919 RNA causes inhibition of translation of respective one or more VGAM1919 host target proteins.

[63338] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1919 gene, herein designated VGAM GENE, on one or more VGAM1919 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63339] It is yet further appreciated that a function of VGAM1919 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1919 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1919 correlate with, and may be deduced from, the identity of the host target genes which VGAM1919 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63340] Nucleotide sequences of the VGAM1919 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1919 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1919 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1919 are further described hereinbelow with reference to Table 1.

[63341] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1919 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1919 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63342] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1919 gene, herein designated VGAM is inhibition of expression of VGAM1919 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1919 correlate with, and may be deduced from, the identity of the target genes which VGAM1919 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63343] Solute Carrier Family 6 (neurotransmitter transporter, creatine), Member 8 (SLC6A8, Accession NM\_005629) is a VGAM1919 host target gene. SLC6A8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A8 BINDING SITE, designated SEQ ID:12147, to the nucleotide sequence of VGAM1919 RNA, herein designated VGAM

RNA, also designated SEQ ID:4630.

[63344] A function of VGAM1919 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, creatine), Member 8 (SLC6A8, Accession NM\_005629). Accordingly, utilities of VGAM1919 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A8. Telomeric Repeat Binding Factor (NIMA-interacting) 1 (TERF1, Accession NM\_017489) is another VGAM1919 host target gene. TERF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TERF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TERF1 BINDING SITE, designated SEQ ID:18953, to the nucleotide sequence of VGAM1919 RNA, herein designated VGAM RNA, also designated SEQ ID:4630.

[63345] Another function of VGAM1919 is therefore inhibition of Telomeric Repeat Binding Factor (NIMA-interacting) 1 (TERF1, Accession NM\_017489), a gene which negatively regulates telomere length, involves in regulation of the mitotic spindle. Accordingly, utilities of VGAM1919 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with TERF1. The function of TERF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM189.Microtubule-actin Crosslinking Factor 1

(MACF1, Accession NM\_012090) is another VGAM1919 host target gene. MACF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MACF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MACF1 BINDING SITE, designated SEQ ID:14376, to the nucleotide sequence of VGAM1919 RNA, herein designated VGAM RNA, also designated SEQ ID:4630.

[63346] Another function of VGAM1919 is therefore inhibition of Microtubule-actin Crosslinking Factor 1 (MACF1, Accession NM\_012090). Accordingly, utilities of VGAM1919 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MACF1. Testis-specific Kinase 2 (TESK2, Accession XM\_032399) is another VGAM1919 host target gene. TESK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by TESK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TESK2 BINDING SITE, designated SEQ ID:31652, to the nucleotide sequence of VGAM1919 RNA, herein designated VGAM RNA, also designated SEQ ID:4630.

[63347] Another function of VGAM1919 is therefore inhibition of Testis-specific Kinase 2 (TESK2, Accession XM\_032399). Accordingly, utilities of VGAM1919 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TESK2. LOC146488 (Accession XM\_047748) is another VGAM1919 host target gene. LOC146488 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146488, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146488 BINDING SITE, designated SEQ ID:35043, to the nucleotide sequence of VGAM1919 RNA, herein designated VGAM RNA, also designated SEQ ID:4630.

[63348] Another function of VGAM1919 is therefore inhibition of

LOC146488 (Accession XM\_047748). Accordingly, utilities of VGAM1919 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146488. LOC152620 (Accession XM\_011108) is another VGAM1919 host target gene. LOC152620 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152620 BINDING SITE, designated SEQ ID:30175, to the nucleotide sequence of VGAM1919 RNA, herein designated VGAM RNA, also designated SEQ ID:4630.

[63349] Another function of VGAM1919 is therefore inhibition of LOC152620 (Accession XM\_011108). Accordingly, utilities of VGAM1919 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152620. LOC158668 (Accession XM\_045161) is another VGAM1919 host target gene. LOC158668 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC158668 BINDING SITE, designated SEQ ID:34378, to the nucleotide sequence of VGAM1919 RNA, herein designated VGAM RNA, also designated SEQ ID:4630.

[63350] Another function of VGAM1919 is therefore inhibition of LOC158668 (Accession XM\_045161). Accordingly, utilities of VGAM1919 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158668. LOC257000 (Accession XM\_172999) is another VGAM1919 host target gene. LOC257000 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257000, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257000 BINDING SITE, designated SEQ ID:46273, to the nucleotide sequence of VGAM1919 RNA, herein designated VGAM RNA, also designated SEQ ID:4630.

[63351] Another function of VGAM1919 is therefore inhibition of LOC257000 (Accession XM\_172999). Accordingly, utilities of VGAM1919 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257000. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1920 (VGAM1920) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63352] VGAM1920 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1920 was detected is described hereinabove with reference to Figs. 1–8.

[63353] VGAM1920 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine Distemper Virus. VGAM1920 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63354] VGAM1920 gene encodes a VGAM1920 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1920 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1920 precursor RNA is designated SEQ ID:1906, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1906 is located at position 12749 relative to the genome of Canine Distemper Virus.

[63355] VGAM1920 precursor RNA folds onto itself, forming VGAM1920 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63356] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1920 folded precursor RNA into VGAM1920 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1920 RNA is designated SEQ ID:4631, and is provided hereinbelow with reference to the sequence listing part.

[63357] VGAM1920 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1920 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1920 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63358] VGAM1920 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1920 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1920 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1920 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1920 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[63359] The complementary binding of VGAM1920 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1920 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1920 host target RNA into VGAM1920 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63360] It is appreciated that VGAM1920 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1920 host target genes. The mRNA of each one of this plurality of VGAM1920 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1920 RNA, herein designated VGAM RNA, and which when bound by VGAM1920 RNA causes inhibition of translation of respective one or more

VGAM1920 host target proteins.

[63361] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1920 gene, herein designated VGAM GENE, on one or more VGAM1920 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63362] It is yet further appreciated that a function of VGAM1920 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1920 include diagnosis, prevention and treatment of viral infection by Canine Distemper Virus.

Specific functions, and accordingly utilities, of VGAM1920 correlate with, and may be deduced from, the identity of the host target genes which VGAM1920 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63363] Nucleotide sequences of the VGAM1920 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1920 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1920 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1920 are further described hereinbelow with reference to Table 1.

[63364] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1920 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1920 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63365] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1920 gene, herein designated VGAM is inhibition of expression of VGAM1920 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1920 correlate with, and may be deduced from, the identity of the target genes which VGAM1920 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63366] Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession NM\_052962) is a VGAM1920 host target gene. IL22RA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL22RA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL22RA2 BINDING SITE, designated SEQ ID:27520, to the nucleotide sequence of VGAM1920 RNA, herein designated VGAM RNA, also designated SEQ ID:4631.

[63367] A function of VGAM1920 is therefore inhibition of Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession NM\_052962), a gene which induces the production of acute-phase reactants. Accordingly, utilities of VGAM1920 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL22RA2. The function of IL22RA2 and its association with various diseases and clinical conditions, has been established by previous



studies, as described hereinabove with reference to VGAM167.DKFZp566D133 (Accession XM\_050005) is another VGAM1920 host target gene. DKFZp566D133 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp566D133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp566D133 BINDING SITE, designated SEQ ID:35542, to the nucleotide sequence of VGAM1920 RNA, herein designated VGAM RNA, also designated SEQ ID:4631.

[63368] Another function of VGAM1920 is therefore inhibition of DKFZp566D133 (Accession XM\_050005). Accordingly, utilities of VGAM1920 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp566D133. FLJ11160 (Accession NM\_018344) is another VGAM1920 host target gene. FLJ11160 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FLJ11160 BINDING SITE, designated SEQ ID:20350, to the nucleotide sequence of VGAM1920 RNA, herein designated VGAM RNA, also designated SEQ ID:4631.

[63369] Another function of VGAM1920 is therefore inhibition of FLJ11160 (Accession NM\_018344). Accordingly, utilities of VGAM1920 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11160. FLJ14936 (Accession NM\_032864) is another VGAM1920 host target gene. FLJ14936 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14936 BINDING SITE, designated SEQ ID:26668, to the nucleotide sequence of VGAM1920 RNA, herein designated VGAM RNA, also designated SEQ ID:4631.

[63370] Another function of VGAM1920 is therefore inhibition of FLJ14936 (Accession NM\_032864). Accordingly, utilities of VGAM1920 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14936. KIAA1522 (Accession XM\_036299) is another VGAM1920 host target gene. KIAA1522 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1522 BINDING SITE, designated SEQ ID:32415, to the nucleotide sequence of VGAM1920 RNA, herein designated VGAM RNA, also designated SEQ ID:4631.

[63371] Another function of VGAM1920 is therefore inhibition of KIAA1522 (Accession XM\_036299). Accordingly, utilities of VGAM1920 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1522. Polymerase I and Transcript Release Factor (PTRF, Accession XM\_032852) is another VGAM1920 host target gene. PTRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTRF BINDING SITE, designated SEQ ID:31781, to the nucleotide sequence of VGAM1920 RNA, herein designated VGAM RNA, also designated SEQ ID:4631.

[63372] Another function of VGAM1920 is therefore inhibition of Polymerase I and Transcript Release Factor (PTRF, Accession XM\_032852). Accordingly, utilities of VGAM1920 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTRF. LOC253959 (Accession XM\_170749) is another VGAM1920 host target gene. LOC253959 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253959, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253959 BINDING SITE, designated SEQ ID:45508, to the nucleotide sequence of VGAM1920 RNA, herein designated VGAM RNA, also designated SEQ ID:4631.

[63373] Another function of VGAM1920 is therefore inhibition of LOC253959 (Accession XM\_170749). Accordingly, utilities of VGAM1920 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253959. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1921 (VGAM1921) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63374] VGAM1921 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1921 was detected is described hereinabove with reference to Figs. 1–8.

[63375] VGAM1921 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine Distemper Virus. VGAM1921 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63376] VGAM1921 gene encodes a VGAM1921 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1921 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1921 precursor RNA is designated SEQ ID:1907, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1907 is located at position 9746 relative to the genome of Canine Distemper Virus.

[63377] VGAM1921 precursor RNA folds onto itself, forming

VGAM1921 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63378] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1921 folded precursor RNA into VGAM1921 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1921 RNA is designated SEQ ID:4632, and is provided hereinbelow with reference to the sequence listing part.

[63379] VGAM1921 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1921 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1921 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[63380] VGAM1921 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1921 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1921 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1921 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1921 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63381] The complementary binding of VGAM1921 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1921 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1921 host target RNA into VGAM1921 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63382] It is appreciated that VGAM1921 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1921 host target genes. The mRNA of each one of this plurality of VGAM1921 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1921 RNA, herein designated VGAM RNA, and which when bound by VGAM1921 RNA causes inhibition of translation of respective one or more VGAM1921 host target proteins.

[63383] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with



specific reference to translational inhibition exerted by VGAM1921 gene, herein designated VGAM GENE, on one or more VGAM1921 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63384] It is yet further appreciated that a function of VGAM1921 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1921 include diagnosis, prevention and treatment of viral infection by Canine Distemper Virus. Specific functions, and accordingly utilities, of VGAM1921 correlate with, and may be deduced from, the identity of the host target genes which VGAM1921 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[63385] Nucleotide sequences of the VGAM1921 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1921 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1921 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1921 are further described hereinbelow with reference to Table 1.

[63386] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1921 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1921 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63387] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1921 gene, herein designated VGAM is inhibition of expression of VGAM1921 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1921 correlate with, and may be deduced from, the identity of the target genes which VGAM1921 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[63388] Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM\_080821) is a VGAM1921 host target gene. C20orf108 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf108 BINDING SITE, designated SEQ ID:28080, to the nucleotide sequence of VGAM1921 RNA, herein designated VGAM RNA, also designated SEQ ID:4632.

[63389] A function of VGAM1921 is therefore inhibition of Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM\_080821). Accordingly, utilities of VGAM1921 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf108. FLJ10891 (Accession NM\_018260) is another VGAM1921 host target gene. FLJ10891 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of FLJ10891 BINDING SITE, designated SEQ ID:20225, to the nucleotide sequence of VGAM1921 RNA, herein designated VGAM RNA, also designated SEQ ID:4632.

[63390] Another function of VGAM1921 is therefore inhibition of FLJ10891 (Accession NM\_018260). Accordingly, utilities of VGAM1921 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10891. FLJ12985 (Accession NM\_024924) is another VGAM1921 host target gene. FLJ12985 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12985, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12985 BINDING SITE, designated SEQ ID:24463, to the nucleotide sequence of VGAM1921 RNA, herein designated VGAM RNA, also designated SEQ ID:4632.

[63391] Another function of VGAM1921 is therefore inhibition of FLJ12985 (Accession NM\_024924). Accordingly, utilities of VGAM1921 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12985. FLJ25416 (Accession NM\_145018) is another

VGAM1921 host target gene. FLJ25416 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ25416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ25416 BINDING SITE, designated SEQ ID:29624, to the nucleotide sequence of VGAM1921 RNA, herein designated VGAM RNA, also designated SEQ ID:4632.

[63392] Another function of VGAM1921 is therefore inhibition of FLJ25416 (Accession NM\_145018). Accordingly, utilities of VGAM1921 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ25416. Potassium Inwardly-rectifying Channel, Subfamily J, Member 2 (KCNJ2, Accession NM\_000891) is another VGAM1921 host target gene. KCNJ2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNJ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ2 BINDING SITE, designated SEQ ID:6589, to the nucleotide sequence of VGAM1921 RNA, herein designated VGAM RNA,

also designated SEQ ID:4632.

[63393] Another function of VGAM1921 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 2 (KCNJ2, Accession NM\_000891). Accordingly, utilities of VGAM1921 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ2. KIAA0798 (Accession NM\_014650) is another VGAM1921 host target gene. KIAA0798 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0798 BINDING SITE, designated SEQ ID:16064, to the nucleotide sequence of VGAM1921 RNA, herein designated VGAM RNA, also designated SEQ ID:4632.

[63394] Another function of VGAM1921 is therefore inhibition of KIAA0798 (Accession NM\_014650). Accordingly, utilities of VGAM1921 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0798. LOC145813 (Accession XM\_096873) is another VGAM1921 host target gene. LOC145813 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC145813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145813 BINDING SITE, designated SEQ ID:40596, to the nucleotide sequence of VGAM1921 RNA, herein designated VGAM RNA, also designated SEQ ID:4632.

[63395] Another function of VGAM1921 is therefore inhibition of LOC145813 (Accession XM\_096873). Accordingly, utilities of VGAM1921 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145813. LOC255624 (Accession XM\_170531) is another VGAM1921 host target gene. LOC255624 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255624 BINDING SITE, designated SEQ ID:45351, to the nucleotide sequence of VGAM1921 RNA, herein designated VGAM RNA, also designated SEQ ID:4632.

[63396] Another function of VGAM1921 is therefore inhibition of LOC255624 (Accession XM\_170531). Accordingly, utilities

of VGAM1921 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255624. LOC64116 (Accession NM\_022154) is another VGAM1921 host target gene. LOC64116 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC64116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC64116 BINDING SITE, designated SEQ ID:22712, to the nucleotide sequence of VGAM1921 RNA, herein designated VGAM RNA, also designated SEQ ID:4632.

[63397] Another function of VGAM1921 is therefore inhibition of LOC64116 (Accession NM\_022154). Accordingly, utilities of VGAM1921 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC64116. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1922 (VGAM1922) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[63398] VGAM1922 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1922 was detected is described hereinabove with reference to Figs. 1–8.

[63399] VGAM1922 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine Distemper Virus. VGAM1922 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63400] VGAM1922 gene encodes a VGAM1922 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1922 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1922 precursor RNA is designated SEQ ID:1908, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1908 is located at position 11765 relative to the genome of Canine Distemper Virus.

[63401] VGAM1922 precursor RNA folds onto itself, forming VGAM1922 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63402] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1922 folded precursor RNA into VGAM1922 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1922 RNA is designated SEQ ID:4633, and is provided hereinbelow with reference to the sequence listing part.

[63403] VGAM1922 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1922 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1922 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[63404] VGAM1922 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1922 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1922 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1922 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1922 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63405] The complementary binding of VGAM1922 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1922 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1922 host target RNA into VGAM1922 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63406] It is appreciated that VGAM1922 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1922 host target genes. The mRNA of each one of this plurality of VGAM1922 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1922 RNA, herein designated VGAM RNA, and which when bound by VGAM1922 RNA causes inhibition of translation of respective one or more VGAM1922 host target proteins.

[63407] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1922 gene, herein designated VGAM GENE, on one or more VGAM1922 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[63408] It is yet further appreciated that a function of VGAM1922 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1922 include diagnosis, prevention and treatment of viral infection by Canine Distemper Virus. Specific functions, and accordingly utilities, of VGAM1922 correlate with, and may be deduced from, the identity of the host target genes which VGAM1922 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63409] Nucleotide sequences of the VGAM1922 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the  
`diced` VGAM1922 RNA, herein designated VGAM RNA,  
and a schematic representation of the secondary folding  
of VGAM1922 folded precursor RNA, herein designated  
VGAM FOLDED PRECURSOR RNA, of VGAM1922 are further  
described hereinbelow with reference to Table 1.

[63410] Nucleotide sequences of host target binding sites, such as  
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of  
Fig. 1, found on VGAM1922 host target RNA, and  
schematic representation of the complementarity of each  
of these host target binding sites to VGAM1922 RNA,  
herein designated VGAM RNA, are described hereinbelow  
with reference to Table 2.

[63411] As mentioned hereinabove with reference to Fig. 1, a  
function of VGAM1922 gene, herein designated VGAM is  
inhibition of expression of VGAM1922 target genes. It is  
appreciated that specific functions, and accordingly utili-  
ties, of VGAM1922 correlate with, and may be deduced  
from, the identity of the target genes which VGAM1922  
binds and inhibits, and the function of these target genes,  
as elaborated hereinbelow.

[63412] Nucleosome Assembly Protein 1-like 4 (NAP1L4, Acces-  
sion NM\_005969) is a VGAM1922 host target gene.

NAP1L4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAP1L4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAP1L4 BINDING SITE, designated SEQ ID:12591, to the nucleotide sequence of VGAM1922 RNA, herein designated VGAM RNA, also designated SEQ ID:4633.

[63413] A function of VGAM1922 is therefore inhibition of Nucleosome Assembly Protein 1-like 4 (NAP1L4, Accession NM\_005969), a gene which may have a role as a histone chaperone. Accordingly, utilities of VGAM1922 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAP1L4. The function of NAP1L4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM949.NDRG Family Member 2 (NDRG2, Accession NM\_016250) is another VGAM1922 host target gene. NDRG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDRG2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG2 BINDING SITE, designated SEQ ID:18379, to the nucleotide sequence of VGAM1922 RNA, herein designated VGAM RNA, also designated SEQ ID:4633.

[63414] Another function of VGAM1922 is therefore inhibition of NDRG Family Member 2 (NDRG2, Accession NM\_016250), a gene which belongs to the ndrg family. Accordingly, utilities of VGAM1922 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG2. The function of NDRG2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1130. Plastin 3 (T isoform) (PLS3, Accession NM\_005032) is another VGAM1922 host target gene. PLS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLS3 BINDING SITE, designated SEQ ID:11472, to the nucleotide sequence of VGAM1922 RNA, herein



designated VGAM RNA, also designated SEQ ID:4633.

[63415] Another function of VGAM1922 is therefore inhibition of Plastin 3 (T isoform) (PLS3, Accession NM\_005032), a gene which binds actin. Accordingly, utilities of VGAM1922 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLS3. The function of PLS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1754. Rhodopsin (opsin 2, rod pigment) (retinitis pigmentosa 4, autosomal dominant) (RHO, Accession NM\_000539) is another VGAM1922 host target gene. RHO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RHO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHO BINDING SITE, designated SEQ ID:6139, to the nucleotide sequence of VGAM1922 RNA, herein designated VGAM RNA, also designated SEQ ID:4633.

[63416] Another function of VGAM1922 is therefore inhibition of Rhodopsin (opsin 2, rod pigment) (retinitis pigmentosa 4, autosomal dominant) (RHO, Accession NM\_000539). Ac-

cordingly, utilities of VGAM1922 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHO. CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM\_054838) is another VGAM1922 host target gene. CSMD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CSMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSMD1 BINDING SITE, designated SEQ ID:36192, to the nucleotide sequence of VGAM1922 RNA, herein designated VGAM RNA, also designated SEQ ID:4633.

[63417] Another function of VGAM1922 is therefore inhibition of CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM\_054838). Accordingly, utilities of VGAM1922 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSMD1. MKP-7 (Accession XM\_039106) is another VGAM1922 host target gene. MKP-7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MKP-7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of MKP-7 BINDING SITE, designated SEQ ID:33006, to the nucleotide sequence of VGAM1922 RNA, herein designated VGAM RNA, also designated SEQ ID:4633.

[63418] Another function of VGAM1922 is therefore inhibition of MKP-7 (Accession XM\_039106). Accordingly, utilities of VGAM1922 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKP-7. Matrix Metalloproteinase 28 (MMP28, Accession NM\_032950) is another VGAM1922 host target gene. MMP28 BINDING SITE1 and MMP28 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MMP28, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP28 BINDING SITE1 and MMP28 BINDING SITE2, designated SEQ ID:26763 and SEQ ID:23594 respectively, to the nucleotide sequence of VGAM1922 RNA, herein designated VGAM RNA, also designated SEQ ID:4633.

[63419] Another function of VGAM1922 is therefore inhibition of Matrix Metalloproteinase 28 (MMP28, Accession

NM\_032950). Accordingly, utilities of VGAM1922 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP28. BCL2-like 2 (BCL2L2, Accession NM\_004050) is another VGAM1923 host target gene. BCL2L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL2L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2L2 BINDING SITE, designated SEQ ID:10266, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63420] Another function of VGAM1923 is therefore inhibition of BCL2-like 2 (BCL2L2, Accession NM\_004050), a gene which promotes cell survival. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2L2. The function of BCL2L2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM431. Cyclin D2 (CCND2, Accession NM\_001759) is another VGAM1923 host target gene.

CCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7519, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63421] Another function of VGAM1923 is therefore inhibition of Cyclin D2 (CCND2, Accession NM\_001759), a gene which is essential for the control of the cell cycle at the G1/s (start) transition. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128.CDK2-associated Protein 1 (CDK2AP1, Accession NM\_004642) is another VGAM1923 host target gene. CDK2AP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDK2AP1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK2AP1 BINDING SITE, designated SEQ ID:11016, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63422] Another function of VGAM1923 is therefore inhibition of CDK2-associated Protein 1 (CDK2AP1, Accession NM\_004642), a gene which negatively regulates CDK2 activity. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK2AP1. The function of CDK2AP1 has been established by previous studies. Todd et al. (1995) isolated an evolutionarily conserved gene that exhibits frequent losses of heterozygosity (LOH) and significant reduction in expression in malignant oral keratinocytes of the hamster (*Mesocricetus auratus*). They symbolized the gene doc-1 for 'deleted in oral cancer.' Transfection of normal doc-1 cDNA into malignant oral keratinocytes reversed the transformed phenotype in the hamster model. Daigo et al. (1997) isolated a human cDNA encoding a 115-amino acid polypeptide that shows 97% identity to the doc-1 gene of the hamster. It also

shows a high degree of homology to a gene induced by TNF-alpha (OMIM Ref. No. 191160) in the mouse. To investigate its possible role in esophageal carcinogenesis, they examined genetic alterations in expression levels of the gene in 13 esophageal carcinoma cell lines and 10 primary esophageal carcinomas. No mutation or reduction of expression was observed in any of the 23 cancer materials examined. By fluorescence in situ hybridization, they mapped the human DOC1 gene to 12q24.31.

[63423] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63424] Daigo, Y.; Suzuki, K.; Maruyama, O.; Miyoshi, Y.; Yasuda, T.; Kabuto, T.; Imaoka, S.; Fujiwara, T.; Takahashi, E.; Fujino, M. A.; Nakamura, Y. : Isolation, mapping, and mutation analysis of a human cDNA homologous to the doc-1 gene of the Chinese hamster, a candidate tumor suppressor for oral cancer. *Genes Chromosomes Cancer* 20: 204-207, 1997. ; and

[63425] Todd, R.; McBride, J.; Tsuji, T.; Donoff, R. B.; Nagai, M.; Chou, M. Y.; Chiang, T.; Wong, D. T. W. : Deleted in oral cancer-1 (doc-1), a novel oral tumor suppressor gene. *FASEB J.* 1362.

[63426] Further studies establishing the function and utilities of CDK2AP1 are found in John Hopkins OMIM database record ID 602198, and in cited publications numbered 1226–1227 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cadherin, EGF LAG Seven-pass G-type Receptor 1 (flamingo homolog, Drosophila) (CELSR1, Accession NM\_014246) is another VGAM1923 host target gene. CELSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CELSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CELSR1 BINDING SITE, designated SEQ ID:15517, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63427] Another function of VGAM1923 is therefore inhibition of Cadherin, EGF LAG Seven-pass G-type Receptor 1 (flamingo homolog, Drosophila) (CELSR1, Accession NM\_014246), a gene which is involved in contact-mediated communication. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CELSR1. The func-



tion of CELSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM459. Chromosome Condensation 1-like (CHC1L, Accession NM\_001268) is another VGAM1923 host target gene. CHC1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHC1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHC1L BINDING SITE, designated SEQ ID:6931, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63428] Another function of VGAM1923 is therefore inhibition of Chromosome Condensation 1-like (CHC1L, Accession NM\_001268). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHC1L. C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 11 (CLECSF11, Accession NM\_130441) is another VGAM1923 host target gene. CLECSF11 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by CLECSF11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF11 BINDING SITE, designated SEQ ID:28200, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63429] Another function of VGAM1923 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 11 (CLECSF11, Accession NM\_130441), a gene which may play a role in ligand internalization and presentation. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF11. The function of CLECSF11 has been established by previous studies. CLONING By screening an EST database for sequences homologous to the CRD of DC immunoreceptor (DCIR; 605306), followed by 5-prime and 3-prime RACE, Arce et al. (2001) obtained a cDNA encoding DLEC. Sequence analysis predicted that DLEC is a 213-amino acid type II integral membrane protein with an N-terminal cytoplasmic tail, a transmembrane region, an extracellular stalk region, and a single C-terminal CRD.

The CRD is 79% identical to that of DCIR and has 3 potential N-glycosylation sites and 1 conserved calcium-binding site that contains a mannose-binding EPN motif. RT-PCR analysis suggested the existence of a splice variant, DLEC-beta. Northern blot analysis did not detect expression of DLEC in immunologic tissues. RT-PCR analysis detected expression of DLEC only in peripheral blood mononuclear cells and immature dendritic cells. Northern blot analysis showed constitutive expression of DLEC in immature monocyte-derived DCs that was downregulated by maturation with lipopolysaccharide but not with tumor necrosis factor (TNF; 191160). By immunoscreening COS cells expressing cDNAs from plasmacytoid dendritic cells (PDCs), Dzionek et al. (2001) obtained a cDNA encoding DLEC, which they designated BDCA2. RT-PCR analysis detected expression of BDCA2 that was restricted to PDCs. Immunofluorescence microscopy and immunohistochemistry demonstrated expression of BDCA2 in CD123 (IL3RA; 308385)-positive tonsillar and lymph node cells. RT-PCR analysis suggested the existence of 5 BDCA2 splice variants, each lacking 1 or 2 exons. Immunoprecipitation and SDS-PAGE analyses showed expression of a 38-kD BDCA2 protein. Functional analysis indicated that BDCA2 mobi-

lizes intracellular calcium. Immunoblot analysis established that anti-BDCA2 triggers protein-tyrosine phosphorylation of PDCs. ELISA showed that BDCA2 ligation inhibits IFNA (OMIM Ref. No. 147660)/IFNB (OMIM Ref. No. 147640) production by cells stimulated with influenza antigens or anti-DNA antibodies.

[63430] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63431] Arce, I.; Roda-Navarro, P.; Montoya, M. C.; Hernanz-Falcon, P.; Puig-Kroger, A.; Fernandez-Ruiz, E. : Molecular and genomic characterization of human DLEC, a novel member of the C-type lectin receptor gene family preferentially expressed on monocyte-derived dendritic cells. *Europ. J. Immun.* 31: 2733-2740, 2001. ; and

[63432] Dzionek, A.; Sohma, Y.; Nagafune, J.; Cella, M.; Colonna, M.; Facchetti, F.; Gunther, G.; Johnston, I.; Lanzavecchia, A.; Nagasaka, T.; Okada, T.; Vermi, W.; Winkels, G.; Yamamoto, T.;

[63433] Further studies establishing the function and utilities of CLECSF11 are found in John Hopkins OMIM database record ID 606677, and in cited publications numbered 5543-5544 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Cytochrome P450, Subfamily I (dioxin-inducible), Polypeptide 1 (glaucoma 3, primary infantile) (CYP1B1, Accession NM\_000104) is another VGAM1923 host target gene. CYP1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP1B1 BINDING SITE, designated SEQ ID:5565, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63434] Another function of VGAM1923 is therefore inhibition of Cytochrome P450, Subfamily I (dioxin-inducible), Polypeptide 1 (glaucoma 3, primary infantile) (CYP1B1, Accession NM\_000104), a gene which participates in the metabolism of a molecule that is a participant in eye development. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP1B1. The function of CYP1B1 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM894.Cytochrome P450, Subfamily XXIV (vitamin D 24-hydroxylase) (CYP24, Accession NM\_000782) is another VGAM1923 host target gene. CYP24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP24 BINDING SITE, designated SEQ ID:6428, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63435] Another function of VGAM1923 is therefore inhibition of Cytochrome P450, Subfamily XXIV (vitamin D 24-hydroxylase) (CYP24, Accession NM\_000782), a gene which induces the differentiation of promyelocytes into monocytes/macrophages. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP24. The function of CYP24 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1204.Dystrophin (muscular dystrophy, Duchenne

and Becker types) (DMD, Accession NM\_000109) is another VGAM1923 host target gene. DMD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DMD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMD BINDING SITE, designated SEQ ID:5572, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63436] Another function of VGAM1923 is therefore inhibition of Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM\_000109), a gene which muscular dystrophy . Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMD. The function of DMD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM218.DNA (cytosine-5-)-methyltransferase 2 (DNMT2, Accession NM\_004412) is another VGAM1923 host target gene. DNMT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

DNMT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT2 BINDING SITE, designated SEQ ID:10672, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63437] Another function of VGAM1923 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 2 (DNMT2, Accession NM\_004412), a gene which may mark specific sequences in the genome . Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT2. The function of DNMT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM177. Diphtheria Toxin Resistance Protein Required For Diphthamide Biosynthesis-like 2 (*S. cerevisiae*) (DPH2L2, Accession NM\_001384) is another VGAM1923 host target gene. DPH2L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DPH2L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPH2L2 BINDING SITE, designated SEQ ID:7058, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63438] Another function of VGAM1923 is therefore inhibition of Diphtheria Toxin Resistance Protein Required For Diphthamide Biosynthesis-like 2 (*S. cerevisiae*) (DPH2L2, Accession NM\_001384), a gene which is required for diphthamide biosynthesis. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPH2L2. The function of DPH2L2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1221. Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM\_005228) is another VGAM1923 host target gene. EGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of EGFR BINDING SITE, designated SEQ ID:11726, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63439] Another function of VGAM1923 is therefore inhibition of Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM\_005228), a gene which is a receptor for egf, but also for other members of the egf family. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFR. The function of EGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229. Coagulation Factor II (thrombin) Receptor-like 3 (F2RL3, Accession NM\_003950) is another VGAM1923 host target gene. F2RL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by F2RL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F2RL3 BINDING SITE, designated SEQ

ID:10084, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63440] Another function of VGAM1923 is therefore inhibition of Coagulation Factor II (thrombin) Receptor-like 3 (F2RL3, Accession NM\_003950), a gene which Protease-activated receptor 4; G protein-coupled receptor that increases phosphoinositide hydrolysis. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F2RL3. The function of F2RL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM193. Fatty-acid-Coenzyme A Ligase, Long-chain 4 (FACL4, Accession NM\_022977) is another VGAM1923 host target gene. FACL4 BINDING SITE1 and FACL4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FACL4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FACL4 BINDING SITE1 and FACL4 BINDING SITE2, designated SEQ ID:23254 and SEQ ID:10764 respectively, to the

nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63441] Another function of VGAM1923 is therefore inhibition of Fatty-acid-Coenzyme A Ligase, Long-chain 4 (FACL4, Accession NM\_022977). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FACL4. G Protein-coupled Receptor 48 (GPR48, Accession NM\_018490) is another VGAM1923 host target gene. GPR48 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR48, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR48 BINDING SITE, designated SEQ ID:20551, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63442] Another function of VGAM1923 is therefore inhibition of G Protein-coupled Receptor 48 (GPR48, Accession NM\_018490), a gene which binds to follicle-stimulating hormone and thyroid-stimulating hormone. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with GPR48. The function of GPR48 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM376. Histone Deacetylase 7A (HDAC7A, Accession NM\_015401) is another VGAM1923 host target gene. HDAC7A BINDING SITE1 and HDAC7A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HDAC7A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC7A BINDING SITE1 and HDAC7A BINDING SITE2, designated SEQ ID:17713 and SEQ ID:18683 respectively, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63443] Another function of VGAM1923 is therefore inhibition of Histone Deacetylase 7A (HDAC7A, Accession NM\_015401). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC7A. Hypoxia-inducible Factor 1, Alpha Subunit (basic helix-loop-helix transcription factor) (HIF1A, Accession NM\_001530) is another VGAM1923 host target gene. HIF1A BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by HIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIF1A BINDING SITE, designated SEQ ID:7268, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63444] Another function of VGAM1923 is therefore inhibition of Hypoxia-inducible Factor 1, Alpha Subunit (basic helix-loop-helix transcription factor) (HIF1A, Accession NM\_001530), a gene which is a basic helix-loop-helix transcription factor and mediates transcriptional responses to hypoxia and dioxin-signaling. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIF1A. The function of HIF1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229. Hormonally Upregulated Neu-associated Kinase (HUNK, Accession NM\_014586) is another VGAM1923 host target gene. HUNK BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by HUNK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HUNK BINDING SITE, designated SEQ ID:15952, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63445] Another function of VGAM1923 is therefore inhibition of Hormonally Upregulated Neu-associated Kinase (HUNK, Accession NM\_014586). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HUNK. Interleukin 8 Receptor, Alpha (IL8RA, Accession NM\_000634) is another VGAM1923 host target gene. IL8RA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL8RA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL8RA BINDING SITE, designated SEQ ID:6267, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63446] Another function of VGAM1923 is therefore inhibition of

Interleukin 8 Receptor, Alpha (IL8RA, Accession NM\_000634), a gene which is the receptor to interleukin-8, which is a powerful neutrophils chemotactic factor. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL8RA. The function of IL8RA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM300. inositol(myo)-1(or 4)-monophosphatase 1 (IMPA1, Accession NM\_005536) is another VGAM1923 host target gene. IMPA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IMPA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMPA1 BINDING SITE, designated SEQ ID:12058, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63447] Another function of VGAM1923 is therefore inhibition of inositol(myo)-1(or 4)-monophosphatase 1 (IMPA1, Accession NM\_005536), a gene which is responsible for the provision of inositol required for synthesis of phos-



phatidylinositol and polyphosphoinositides. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMPA1. The function of IMPA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM134. Insulinoma-associated 1 (INSM1, Accession NM\_002196) is another VGAM1923 host target gene. INSM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INSM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INSM1 BINDING SITE, designated SEQ ID:7952, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63448] Another function of VGAM1923 is therefore inhibition of Insulinoma-associated 1 (INSM1, Accession NM\_002196). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INSM1. MAD, Mothers Against Decapentaplegic Homolog 7 (Drosophila) (MADH7, Accession

NM\_005904) is another VGAM1923 host target gene.

MADH7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MADH7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADH7 BINDING SITE, designated SEQ ID:12525, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63449] Another function of VGAM1923 is therefore inhibition of MAD, Mothers Against Decapentaplegic Homolog 7 (Drosophila) (MADH7, Accession NM\_005904), a gene which may affect transcription in response to TGF-beta superfamily signaling pathways, inhibits BMP/Smad1 (MADH1) signaling. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADH7. The function of MADH7 has been established by previous studies. Lallemand et al. (2001) showed that cells stably expressing SMAD7 had increased susceptibility to apoptosis induced by TGFB (OMIM Ref. No. 190180), TNFA (OMIM Ref. No. 191160), serum withdrawal, or loss of cell adhesion

(anoikis). SMAD7 decreased NFkB (OMIM Ref. No. 164011) activity, providing a mechanism for the increased apoptosis. Stable expression of RAS (OMIM Ref. No. 190020) suppressed SMAD7 inhibition of NFkB and SMAD7 potentiation of apoptosis. Scleroderma is a chronic systemic disease that leads to fibrosis of the skin and other affected organs. TGFB has been implicated in the pathogenesis of scleroderma. SMAD proteins function as signaling transducers downstream from TGFB receptors. Dong et al. (2002) investigated the signaling components of the TGFB pathway and TGFB activity in scleroderma lesions in vivo and in scleroderma fibroblasts in vitro. Basal level and TGFB-inducible expression of SMAD7 were selectively decreased, whereas SMAD3 (OMIM Ref. No. 603109) expression was increased both in scleroderma skin and in explanted scleroderma fibroblasts in culture. TGFB signaling events were increased in scleroderma fibroblasts relative to normal fibroblasts. In vitro adenoviral gene transfer with SMAD7 restored normal TGFB signaling in scleroderma fibroblasts. These results suggested that alterations in the SMAD pathway, including marked SMAD7 deficiency and SMAD3 upregulation, may be responsible for TGFB hyperresponsiveness observed in scleroderma

- [63450] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [63451] Lallemand, F.; Mazars, A.; Prunier, C.; Bertrand, F.; Kornprost, M.; Gallea, S.; Roman-Roman, S.; Cherqui, G.; Atfi, A. : Smad7 inhibits the survival nuclear factor kappa-B and potentiates apoptosis in epithelial cells. *Oncogene* 20: 879–884, 2001. ; and
- [63452] Dong, C.; Zhu, S.; Wang, T.; Yoon, W.; Li, Z.; Alvarez, R. J.; ten Dijke, P.; White, B.; Wigley, F. M.; Goldschmidt-Clermont, P. J. : Deficient Smad7 expression: a putative molecular defec.
- [63453] Further studies establishing the function and utilities of MADH7 are found in John Hopkins OMIM database record ID 602932, and in cited publications numbered 7970–797 and 7753 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. MAX Protein (MAX, Accession NM\_002382) is another VGAM1923 host target gene. MAX BINDING SITE1 through MAX BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAX, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MAX BINDING SITE1 through MAX BINDING SITE4, designated SEQ ID:8201, SEQ ID:29718, SEQ ID:29720 and SEQ ID:29723 respectively, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63454] Another function of VGAM1923 is therefore inhibition of MAX Protein (MAX, Accession NM\_002382), a gene which interacts specifically with the MYC (190080) protein . Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAX. The function of MAX has been established by previous studies. The MAX gene encodes a protein that interacts specifically with the MYC (OMIM Ref. No. 190080) protein to form a heterodimer with high affinity for the specific cognate DNA binding site of MYC. Wagner et al. (1992) demonstrated that 2 species of RNA hybridized specifically to a MAX cDNA probe in all human and murine cell lines tested. Unlike MYC, the steady state level of MAX RNA was not significantly modulated with respect to proliferation or differentiation. Unlike MYC RNA, MAX RNA was relatively stable with a half-life of more than 3 hours, and therefore it did not exhibit the charac-

teristic short half-life of RNAs encoded by most immediate early genes. The predicted tertiary structure of MAX closely resembles that of MYC, and it was on the basis of the basic/helix-loop-helix/leucine-zipper homology that Prendergast et al. (1991) cloned the cDNA encoding MAX. Zervos et al. (1995) described MIX2 (OMIM Ref. No. 600601), a protein that interacts with the MAX protein. Grandori et al. (1996) identified DDX18 (OMIM Ref. No. 606355) as a direct in vivo target of Myc and Max and hypothesized that Myc may exert its effects on cell behavior through proteins that affect RNA structure and metabolism. By fluorescence in situ chromosomal hybridization, Wagner et al. (1992) demonstrated that the MAX gene is located in band 14q23. This region of chromosome 14 is involved in deletions in B-cell chronic lymphocytic leukemia and malignant lymphomas and in the 12;14 translocation in uterine leiomyomas. Gilladoga et al. (1992) similarly mapped the MAX gene to 14q22-q24 by isotopic in situ hybridization and to mouse chromosome 12 in region D.

[63455] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63456] Wagner, A. J.; Le Beau, M. M.; Diaz, M. O.; Hay, N. : Expression, regulation, and chromosomal localization of the Max gene. Proc. Nat. Acad. Sci. 89: 3111–3115, 1992. ; and

[63457] Prendergast, G. C.; Lawe, D.; Ziff, E. B. : Association of Myn, the murine homolog of Max, with c-Myc stimulates methylation-sensitive DNA binding and Ras cotransformation. Cell 65: 395–.

[63458] Further studies establishing the function and utilities of MAX are found in John Hopkins OMIM database record ID 154950, and in cited publications numbered 2965–2967, 1109 and 11099–11101 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nescient Helix Loop Helix 1 (NHLH1, Accession NM\_005598) is another VGAM1923 host target gene. NHLH1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NHLH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NHLH1 BINDING SITE, designated SEQ ID:12126, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ

ID:4634.

[63459] Another function of VGAM1923 is therefore inhibition of Nescient Helix Loop Helix 1 (NHLH1, Accession NM\_005598), a gene which may have a role in development of the nervous system. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NHLH1. The function of NHLH1 has been established by previous studies. Begley et al. (1992) identified a novel member of the HLH family based on its hybridization to SCL. SCL, also called TAL1, had been identified because of its involvement in a 1;14 translocation in a stem cell leukemia; it is disrupted in about one-fourth of cases of T-cell acute lymphoblastic leukemia. The novel gene was referred to as NSCL because of its expression in the developing nervous system. Murine Nscl cDNA clones had a coding region of 399 basepairs, predicting a protein of 14.8 kD. The nucleotide sequence showed 71% identity and the amino acid sequence 61% identity to murine Scl in the HLH domain. Animal model experiments lend further support to the function of NHLH1. Cogliati et al. (2002) developed Nhlh1 null mice. Homozygous mutant mice were predisposed to premature, adult-onset, unexpected death. Elec-



trocardiograms revealed decreased heart rate variability, stress-induced arrhythmia, and impaired baroreceptor sensitivity. Heterozygosity for the closely related transcription factor *Nhlh2* increased the severity of the *Nhlh1* null phenotype. No signs of primary cardiac structural or conduction abnormalities were revealed in the *Nhlh1* null mice. The pattern of altered heart rhythm observed in basal and experimental stress conditions suggested that a deficient parasympathetic tone contributed to the arrhythmia in the *Nhlh1* null mice. Supporting their conclusion, Cogliati et al. (2002) found that *Nhlh1* was expressed in the developing brain stem and vagal nuclei of wildtype mice.

[63460] It is appreciated that the abovementioned animal model for NHLH1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[63461] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63462] Begley, C. G.; Lipkowitz, S.; Gobel, V.; Mahon, K. A.; Bertness, V.; Green, A. R.; Gough, N. M.; Kirsch, I. R. : Molecular characterization of NSCL, a gene encoding a helix-

loop-helix protein expressed in the developing nervous system. Proc. Nat. Acad. Sci. 89: 38-42, 1992. ; and

[63463] Cogliati, T.; Good, D. J.; Haigney, M.; Delgado-Romero, P.; Eckhaus, M. A.; Koch, W. J.; Kirsch, I. R. : Predisposition to arrhythmia and autonomic dysfunction in Nhlh1-deficient mice. M.

[63464] Further studies establishing the function and utilities of NHLH1 are found in John Hopkins OMIM database record ID 162360, and in cited publications numbered 11104-11108 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. NHP2 Non-histone Chromosome Protein 2-like 1 (*S. cerevisiae*) (NHP2L1, Accession NM\_005008) is another VGAM1923 host target gene. NHP2L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NHP2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NHP2L1 BINDING SITE, designated SEQ ID:11445, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63465] Another function of VGAM1923 is therefore inhibition of

NHP2 Non-histone Chromosome Protein 2-like 1 (*S. cerevisiae*) (NHP2L1, Accession NM\_005008), a gene which may play a role in the late stage of spliceosome assembly. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NHP2L1. The function of NHP2L1 has been established by previous studies. In the course of sequencing cDNA clones from fetal brain cDNA libraries, Saito et al. (1996) isolated a gene that encodes a protein highly homologous to NHP2 from *Saccharomyces cerevisiae* (Kolodrubetz and Burgum, 1991). NHP2 is a high-mobility group (HMG)-like protein which is located in the nucleus, although it shows weak homology to some ribosomal proteins. The cDNA cloned by Saito et al. (1996), symbolized NHP2L1, was expressed in all human tissues examined and was localized to 12q24.3 by fluorescence in situ hybridization.

[63466] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63467] Kolodrubetz, D.; Burgum, A. : Sequence and genetic analysis of NHP2: a moderately abundant high mobility group-like nuclear protein with an essential function in *Saccha-*

romyces cerevisiae. Yeast 7: 79–90, 1991. ; and

[63468] Saito, H.; Fujiwara, T.; Shin, S.; Okui, K.; Nakamura, Y. : Cloning and mapping of a human novel cDNA (NHP2L1) that encodes a protein highly homologous to yeast nuclear protein NHP2. Cy.

[63469] Further studies establishing the function and utilities of NHP2L1 are found in John Hopkins OMIM database record ID 601304, and in cited publications numbered 6510–6511 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nuclear Receptor Subfamily 3, Group C, Member 2 (NR3C2, Accession NM\_000901) is another VGAM1923 host target gene. NR3C2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NR3C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR3C2 BINDING SITE, designated SEQ ID:6598, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63470] Another function of VGAM1923 is therefore inhibition of Nuclear Receptor Subfamily 3, Group C, Member 2

(NR3C2, Accession NM\_000901), a gene which is to increase ion and water transport and thus raise extracellular fluid volume and blood pressure and lower potassium levels. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR3C2. The function of NR3C2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM186. Period Homolog 2 (Drosophila) (PER2, Accession NM\_022817) is another VGAM1923 host target gene. PER2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER2 BINDING SITE, designated SEQ ID:23093, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63471] Another function of VGAM1923 is therefore inhibition of Period Homolog 2 (Drosophila) (PER2, Accession NM\_022817), a gene which Period homolog 2; putative circadian clock protein; has a PAS dimerization domain.

Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER2. The function of PER2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. RAB11A, Member RAS Oncogene Family (RAB11A, Accession NM\_004663) is another VGAM1923 host target gene. RAB11A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB11A BINDING SITE, designated SEQ ID:11034, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63472] Another function of VGAM1923 is therefore inhibition of RAB11A, Member RAS Oncogene Family (RAB11A, Accession NM\_004663). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB11A. RAB6A, Member RAS Oncogene Family (RAB6A, Accession NM\_002869) is another VGAM1923 host target gene. RAB6A BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAB6A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB6A BINDING SITE, designated SEQ ID:8777, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63473] Another function of VGAM1923 is therefore inhibition of RAB6A, Member RAS Oncogene Family (RAB6A, Accession NM\_002869), a gene which is involved in protein trafficking. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB6A. The function of RAB6A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. Arginine-glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM\_012102) is another VGAM1923 host target gene. RERE BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RERE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of RERE BINDING SITE, designated SEQ ID:14409, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63474] Another function of VGAM1923 is therefore inhibition of Arginine–glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM\_012102), a gene which binds DRPLA and locates in the nucleus. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RERE. The function of RERE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51.Sodium Channel, Voltage–gated, Type IV, Alpha Polypeptide (SCN4A, Accession NM\_000334) is another VGAM1923 host target gene. SCN4A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SCN4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN4A BINDING SITE, designated SEQ ID:5891, to the nucleotide sequence of



VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63475] Another function of VGAM1923 is therefore inhibition of Sodium Channel, Voltage-gated, Type IV, Alpha Polypeptide (SCN4A, Accession NM\_000334). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN4A. Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM\_003038) is another VGAM1923 host target gene. SLC1A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A4 BINDING SITE, designated SEQ ID:8998, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63476] Another function of VGAM1923 is therefore inhibition of Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM\_003038), a gene which transports alanine, serine, cysteine, and

threonine. exhibits sodium dependence. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A4. The function of SLC1A4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM859. Synaptosomal-associated Protein, 23kDa (SNAP23, Accession NM\_003825) is another VGAM1923 host target gene. SNAP23 BINDING SITE1 and SNAP23 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SNAP23, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAP23 BINDING SITE1 and SNAP23 BINDING SITE2, designated SEQ ID:9920 and SEQ ID:28285 respectively, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63477] Another function of VGAM1923 is therefore inhibition of Synaptosomal-associated Protein, 23kDa (SNAP23, Accession NM\_003825), a gene which is essential component of the high affinity receptor for the general membrane fusion

machinery. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAP23. The function of SNAP23 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1533. Synaptotagmin I (SYT1, Accession NM\_005639) is another VGAM1923 host target gene. SYT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYT1 BINDING SITE, designated SEQ ID:12170, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63478] Another function of VGAM1923 is therefore inhibition of Synaptotagmin I (SYT1, Accession NM\_005639), a gene which may have a regulatory role in the membrane interactions during trafficking of synaptic vesicles at the active zone of the synapse. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYT1. The function

of SYT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM739. Transcription Factor 8 (represses interleukin 2 expression) (TCF8, Accession NM\_030751) is another VGAM1923 host target gene. TCF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF8 BINDING SITE, designated SEQ ID:25038, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63479] Another function of VGAM1923 is therefore inhibition of Transcription Factor 8 (represses interleukin 2 expression) (TCF8, Accession NM\_030751), a gene which may be responsible for transcriptional repression of the il-2 gene and regulates the promoter activity of the atp1a1 gene. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF8. The function of TCF8 and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM166. Tumor Necrosis Factor (ligand) Superfamily, Member 9 (TNFSF9, Accession NM\_003811) is another VGAM1923 host target gene. TNFSF9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFSF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF9 BINDING SITE, designated SEQ ID:9902, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63480] Another function of VGAM1923 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 9 (TNFSF9, Accession NM\_003811). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFSF9. Visual System Homeobox 1 Homolog, CHX10-like (zebrafish) (VSX1, Accession NM\_014588) is another VGAM1923 host target gene. VSX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VSX1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VSX1 BINDING SITE, designated SEQ ID:15956, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63481] Another function of VGAM1923 is therefore inhibition of Visual System Homeobox 1 Homolog, CHX10-like (zebrafish) (VSX1, Accession NM\_014588), a gene which is implicated in ocular development. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VSX1. The function of VSX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM665.WSX1 (Accession NM\_004843) is another VGAM1923 host target gene. WSX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by WSX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WSX1 BINDING SITE, designated SEQ ID:11256, to the nucleotide sequence of

VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63482] Another function of VGAM1923 is therefore inhibition of WSX1 (Accession NM\_004843), a gene which is a member of the class I cytokine receptor family and involved in the modulation of the immune response. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WSX1. The function of WSX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1125. Tyrosine

3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Eta Polypeptide (YWHAH, Accession NM\_003405) is another VGAM1923 host target gene.

YWHAH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YWHAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of YWHAH BINDING SITE, designated SEQ ID:9439, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ

ID:4634.

[63483] Another function of VGAM1923 is therefore inhibition of Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Eta Polypeptide (YWHAH, Accession NM\_003405), a gene which activates tyrosine and tryptophan hydroxylases in the presence of and strongly activates protein kinase c. Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YWHAH. The function of YWHAH has been established by previous studies. Protein 14-3-3 is a protein kinase-dependent activator of tyrosine and tryptophan hydroxylases (191290, 191060) and an endogenous inhibitor of protein kinase C (OMIM Ref. No. 176960). It was first described as a brain-specific bovine protein. It consists of acidic dimeric subunits of about 27 kD. Immunohistochemical analyses showed that the 14-3-3 protein is located exclusively in the cytoplasm of neurons in the cerebral cortex and is axonally transported to the nerve terminals. Electrophoresis and chromatography demonstrated that the 14-3-3 protein exists in at least 7 distinct forms: alpha, beta, gamma, delta, epsilon, zeta, and eta. Watanabe et al. (1994) found mRNA corresponding to an



eighth subtype, which they termed theta, in rat brain. The mRNA theta subtype was found in the gray matter of cerebellar cortex and the hippocampus, as well as in white matter where cell bodies of glial cells predominate. In contrast, mRNA of the zeta subtype was distributed widely in the brain gray matter with high levels of transcripts in the neocortex, hippocampus, caudate-putamen, thalamus, cerebellar cortex, and several brain stem nuclei. A human protein with phospholipase A2 activity was shown to be the zeta subtype of the 14-3-3 protein (Zupan et al., 1992). The gene is also symbolized YWHAH. Muratake et al. (1996) determined that the human YWHAH gene has 2 exons separated by an intron of approximately 8 kb. Using S1 nuclease mapping, primer extension, and RACE PCR, Muratake et al. (1996) identified the transcription initiation site. They also identified several regulatory element sequences, including CRE, in the 5-prime noncoding region. Muratake et al. (1996) noted that the presence of a CRE binding element may indicate that this gene is involved in brain responses to narcotics. The authors also found changes in a 7-bp repeat sequence (GCCTGCA) located in the noncoding region of exon 1 and they speculated that these changes, or other changes in the se-

quence of this gene, may be associated with neuropsychiatric disorders.

[63484] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63485] Muratake, T.; Hayashi, S.; Ichikawa, T.; Kumanishi, T.; Ichimura, Y.; Kuwano, R.; Isobe, T.; Wang, Y.; Minoshima, S.; Shimizu, N.; Takahashi, Y. : Structural organization and chromosomal assignment of the human 14-3-3-eta chain gene (YWHAH). Genomics 36: 63-69, 1996. ; and

[63486] Zupan, L. A.; Steffens, D. L.; Berry, C. A.; Landt, M.; Gross, R. W. : Cloning and expression of a human 14-3-3 protein mediating phospholipolysis. J. Biol. Chem. 267: 8707-8710, 1992.

[63487] Further studies establishing the function and utilities of YWHAH are found in John Hopkins OMIM database record ID 113508, and in cited publications numbered 4188-4193 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248) is another VGAM1923 host target gene. AKAP11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

AKAP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP11 BINDING SITE, designated SEQ ID:18369, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63488] Another function of VGAM1923 is therefore inhibition of A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP11. AP1S3 (Accession XM\_059421) is another VGAM1923 host target gene. AP1S3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP1S3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP1S3 BINDING SITE, designated SEQ ID:36987, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63489] Another function of VGAM1923 is therefore inhibition of

AP1S3 (Accession XM\_059421). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1S3. ARPP-19 (Accession NM\_006628) is another VGAM1923 host target gene. ARPP-19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARPP-19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARPP-19 BINDING SITE, designated SEQ ID:13426, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63490] Another function of VGAM1923 is therefore inhibition of ARPP-19 (Accession NM\_006628). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARPP-19. ATPase, H<sup>+</sup> Transporting, Lysosomal 56/58kDa, V1 Subunit B, Isoform 2 (ATP6V1B2, Accession NM\_001693) is another VGAM1923 host target gene. ATP6V1B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP6V1B2, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP6V1B2 BINDING SITE, designated SEQ ID:7415, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63491] Another function of VGAM1923 is therefore inhibition of ATPase, H<sup>+</sup> Transporting, Lysosomal 56/58kDa, V1 Subunit B, Isoform 2 (ATP6V1B2, Accession NM\_001693). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP6V1B2. BLP2 (Accession NM\_025141) is another VGAM1923 host target gene. BLP2 BINDING SITE1 and BLP2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BLP2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLP2 BINDING SITE1 and BLP2 BINDING SITE2, designated SEQ ID:24780 and SEQ ID:27800 respectively, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63492] Another function of VGAM1923 is therefore inhibition of BLP2 (Accession NM\_025141). Accordingly, utilities of

VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLP2. Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM\_080821) is another VGAM1923 host target gene. C20orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf108 BINDING SITE, designated SEQ ID:28088, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63493] Another function of VGAM1923 is therefore inhibition of Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM\_080821). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf108. Chromosome 20 Open Reading Frame 140 (C20orf140, Accession NM\_144628) is another VGAM1923 host target gene. C20orf140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf140, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf140 BINDING SITE, designated SEQ ID:29443, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63494] Another function of VGAM1923 is therefore inhibition of Chromosome 20 Open Reading Frame 140 (C20orf140, Accession NM\_144628). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf140. Chromosome 20 Open Reading Frame 3 (C20orf3, Accession XM\_042765) is another VGAM1923 host target gene. C20orf3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf3 BINDING SITE, designated SEQ ID:33766, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63495] Another function of VGAM1923 is therefore inhibition of

Chromosome 20 Open Reading Frame 3 (C20orf3, Accession XM\_042765). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf3. Chromosome 20 Open Reading Frame 81 (C20orf81, Accession NM\_022760) is another VGAM1923 host target gene. C20orf81 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C20orf81, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf81 BINDING SITE, designated SEQ ID:23004, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63496] Another function of VGAM1923 is therefore inhibition of Chromosome 20 Open Reading Frame 81 (C20orf81, Accession NM\_022760). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf81. CDW92 (Accession NM\_080546) is another VGAM1923 host target gene. CDW92 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by



CDW92, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDW92 BINDING SITE, designated SEQ ID:27868, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63497] Another function of VGAM1923 is therefore inhibition of CDW92 (Accession NM\_080546). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDW92. CED-6 (Accession NM\_016315) is another VGAM1923 host target gene. CED-6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CED-6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CED-6 BINDING SITE, designated SEQ ID:18433, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63498] Another function of VGAM1923 is therefore inhibition of CED-6 (Accession NM\_016315). Accordingly, utilities of

VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CED-6. CHCR (Accession NM\_018388) is another VGAM1923 host target gene. CHCR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHCR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHCR BINDING SITE, designated SEQ ID:20422, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63499] Another function of VGAM1923 is therefore inhibition of CHCR (Accession NM\_018388). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHCR. DCOHM (Accession NM\_032151) is another VGAM1923 host target gene. DCOHM BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DCOHM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCOHM BINDING SITE,

designated SEQ ID:25848, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63500] Another function of VGAM1923 is therefore inhibition of DCOHM (Accession NM\_032151). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCOHM. DKFZP434C131 (Accession XM\_044630) is another VGAM1923 host target gene. DKFZP434C131 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434C131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C131 BINDING SITE, designated SEQ ID:34245, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63501] Another function of VGAM1923 is therefore inhibition of DKFZP434C131 (Accession XM\_044630). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C131. DKFZp761G0313 (Accession

XM\_038026) is another VGAM1923 host target gene. DKFZp761G0313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761G0313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761G0313 BINDING SITE, designated SEQ ID:32742, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63502] Another function of VGAM1923 is therefore inhibition of DKFZp761G0313 (Accession XM\_038026). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761G0313. DKFZp762M136 (Accession XM\_035635) is another VGAM1923 host target gene. DKFZp762M136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762M136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762M136 BINDING SITE, designated SEQ ID:32304, to the nucleotide sequence of

VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63503] Another function of VGAM1923 is therefore inhibition of DKFZp762M136 (Accession XM\_035635). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762M136. EDR2 (Accession XM\_018136) is another VGAM1923 host target gene. EDR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EDR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDR2 BINDING SITE, designated SEQ ID:30340, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63504] Another function of VGAM1923 is therefore inhibition of EDR2 (Accession XM\_018136). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDR2. EFA6R (Accession NM\_015310) is another VGAM1923 host target gene. EFA6R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by EFA6R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFA6R BINDING SITE, designated SEQ ID:17626, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63505] Another function of VGAM1923 is therefore inhibition of EFA6R (Accession NM\_015310). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFA6R. ESDN (Accession NM\_080927) is another VGAM1923 host target gene. ESDN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESDN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESDN BINDING SITE, designated SEQ ID:28154, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63506] Another function of VGAM1923 is therefore inhibition of ESDN (Accession NM\_080927). Accordingly, utilities of

VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESDN. FLJ00007 (Accession XM\_048928) is another VGAM1923 host target gene. FLJ00007 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ00007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00007 BINDING SITE, designated SEQ ID:35312, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63507] Another function of VGAM1923 is therefore inhibition of FLJ00007 (Accession XM\_048928). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00007. FLJ12587 (Accession NM\_022480) is another VGAM1923 host target gene. FLJ12587 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12587, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12587

BINDING SITE, designated SEQ ID:22852, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63508] Another function of VGAM1923 is therefore inhibition of FLJ12587 (Accession NM\_022480). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12587. FLJ13055 (Accession NM\_022737) is another VGAM1923 host target gene. FLJ13055 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13055, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13055 BINDING SITE, designated SEQ ID:22945, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63509] Another function of VGAM1923 is therefore inhibition of FLJ13055 (Accession NM\_022737). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13055. FLJ13315 (Accession NM\_025005) is another VGAM1923 host target gene. FLJ13315 BINDING SITE is



HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13315, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13315 BINDING SITE, designated SEQ ID:24577, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63510] Another function of VGAM1923 is therefore inhibition of FLJ13315 (Accession NM\_025005). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13315. FLJ13962 (Accession NM\_024862) is another VGAM1923 host target gene. FLJ13962 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13962 BINDING SITE, designated SEQ ID:24299, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63511] Another function of VGAM1923 is therefore inhibition of

FLJ13962 (Accession NM\_024862). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13962. FLJ14084 (Accession NM\_021637) is another VGAM1923 host target gene. FLJ14084 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14084 BINDING SITE, designated SEQ ID:22286, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63512] Another function of VGAM1923 is therefore inhibition of FLJ14084 (Accession NM\_021637). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14084. FLJ20312 (Accession NM\_017761) is another VGAM1923 host target gene. FLJ20312 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ20312 BINDING SITE, designated SEQ ID:19376, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63513] Another function of VGAM1923 is therefore inhibition of FLJ20312 (Accession NM\_017761). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20312. FLJ20445 (Accession NM\_017824) is another VGAM1923 host target gene. FLJ20445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20445 BINDING SITE, designated SEQ ID:19483, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63514] Another function of VGAM1923 is therefore inhibition of FLJ20445 (Accession NM\_017824). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20445. FLJ22794 (Accession XM\_166220) is another

VGAM1923 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44034, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63515] Another function of VGAM1923 is therefore inhibition of FLJ22794 (Accession XM\_166220). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. FLJ32783 (Accession NM\_144968) is another VGAM1923 host target gene. FLJ32783 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32783, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32783 BINDING SITE, designated SEQ ID:29584, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63516] Another function of VGAM1923 is therefore inhibition of FLJ32783 (Accession NM\_144968). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32783. GL004 (Accession XM\_038373) is another VGAM1923 host target gene. GL004 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GL004, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GL004 BINDING SITE, designated SEQ ID:32828, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63517] Another function of VGAM1923 is therefore inhibition of GL004 (Accession XM\_038373). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GL004. HSJ1 (Accession NM\_006736) is another VGAM1923 host target gene. HSJ1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HSJ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of HSJ1 BINDING SITE, designated SEQ ID:13588, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63518] Another function of VGAM1923 is therefore inhibition of HSJ1 (Accession NM\_006736). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSJ1. IBTK (Accession XM\_041401) is another VGAM1923 host target gene. IBTK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IBTK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IBTK BINDING SITE, designated SEQ ID:33518, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63519] Another function of VGAM1923 is therefore inhibition of IBTK (Accession XM\_041401). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IBTK.

KIAA0016 (Accession NM\_014765) is another VGAM1923 host target gene. KIAA0016 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0016 BINDING SITE, designated SEQ ID:16533, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63520] Another function of VGAM1923 is therefore inhibition of KIAA0016 (Accession NM\_014765). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0016. KIAA0090 (Accession XM\_114045) is another VGAM1923 host target gene. KIAA0090 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0090, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0090 BINDING SITE, designated SEQ ID:42653, to the nucleotide sequence of VGAM1923 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4634.

[63521] Another function of VGAM1923 is therefore inhibition of KIAA0090 (Accession XM\_114045). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0090. KIAA0152 (Accession NM\_014730) is another VGAM1923 host target gene. KIAA0152 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0152 BINDING SITE, designated SEQ ID:16338, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63522] Another function of VGAM1923 is therefore inhibition of KIAA0152 (Accession NM\_014730). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0152. KIAA0285 (Accession NM\_014807) is another VGAM1923 host target gene. KIAA0285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0285, corresponding to



a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0285 BINDING SITE, designated SEQ ID:16748, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63523] Another function of VGAM1923 is therefore inhibition of KIAA0285 (Accession NM\_014807). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0285. KIAA0459 (Accession XM\_027862) is another VGAM1923 host target gene. KIAA0459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0459 BINDING SITE, designated SEQ ID:30577, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63524] Another function of VGAM1923 is therefore inhibition of KIAA0459 (Accession XM\_027862). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0459. KIAA0495 (Accession XM\_031397) is another VGAM1923 host target gene. KIAA0495 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0495 BINDING SITE, designated SEQ ID:31361, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63525] Another function of VGAM1923 is therefore inhibition of KIAA0495 (Accession XM\_031397). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0495. KIAA0574 (Accession XM\_045076) is another VGAM1923 host target gene. KIAA0574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0574 BINDING SITE, designated SEQ ID:34346, to the

nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63526] Another function of VGAM1923 is therefore inhibition of KIAA0574 (Accession XM\_045076). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0574. KIAA0680 (Accession NM\_014721) is another VGAM1923 host target gene. KIAA0680 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0680, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0680 BINDING SITE, designated SEQ ID:16285, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63527] Another function of VGAM1923 is therefore inhibition of KIAA0680 (Accession NM\_014721). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0680. KIAA0800 (Accession NM\_014703) is another VGAM1923 host target gene. KIAA0800 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by KIAA0800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0800 BINDING SITE, designated SEQ ID:16238, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63528] Another function of VGAM1923 is therefore inhibition of KIAA0800 (Accession NM\_014703). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0800. KIAA0871 (Accession NM\_014961) is another VGAM1923 host target gene. KIAA0871 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0871 BINDING SITE, designated SEQ ID:17333, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63529] Another function of VGAM1923 is therefore inhibition of KIAA0871 (Accession NM\_014961). Accordingly, utilities

of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0871. KIAA1096 (Accession XM\_043678) is another VGAM1923 host target gene. KIAA1096 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1096 BINDING SITE, designated SEQ ID:33997, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63530] Another function of VGAM1923 is therefore inhibition of KIAA1096 (Accession XM\_043678). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1096. KIAA1145 (Accession XM\_037790) is another VGAM1923 host target gene. KIAA1145 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1145, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1145 BINDING SITE, designated SEQ ID:32683, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63531] Another function of VGAM1923 is therefore inhibition of KIAA1145 (Accession XM\_037790). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1145. KIAA1198 (Accession XM\_032674) is another VGAM1923 host target gene. KIAA1198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1198 BINDING SITE, designated SEQ ID:31713, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63532] Another function of VGAM1923 is therefore inhibition of KIAA1198 (Accession XM\_032674). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. KIAA1203 (Accession XM\_049683) is another VGAM1923 host target gene. KIAA1203 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1203, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1203 BINDING SITE, designated SEQ ID:35471, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63533] Another function of VGAM1923 is therefore inhibition of KIAA1203 (Accession XM\_049683). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1203. KIAA1209 (Accession XM\_027307) is another VGAM1923 host target gene. KIAA1209 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1209, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1209 BINDING SITE, designated SEQ ID:30472, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63534] Another function of VGAM1923 is therefore inhibition of

KIAA1209 (Accession XM\_027307). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1209. KIAA1277 (Accession XM\_035114) is another VGAM1923 host target gene. KIAA1277 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1277 BINDING SITE, designated SEQ ID:32206, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63535] Another function of VGAM1923 is therefore inhibition of KIAA1277 (Accession XM\_035114). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1277. KIAA1301 (Accession XM\_038999) is another VGAM1923 host target gene. KIAA1301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the



complementarity of the nucleotide sequences of KIAA1301 BINDING SITE, designated SEQ ID:32979, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63536] Another function of VGAM1923 is therefore inhibition of KIAA1301 (Accession XM\_038999). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1301. KIAA1497 (Accession XM\_041431) is another VGAM1923 host target gene. KIAA1497 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1497 BINDING SITE, designated SEQ ID:33530, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63537] Another function of VGAM1923 is therefore inhibition of KIAA1497 (Accession XM\_041431). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1497. KIAA1677 (Accession XM\_040383) is another

VGAM1923 host target gene. KIAA1677 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1677, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1677 BINDING SITE, designated SEQ ID:33293, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63538] Another function of VGAM1923 is therefore inhibition of KIAA1677 (Accession XM\_040383). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1677. KIAA1679 (Accession XM\_046570) is another VGAM1923 host target gene. KIAA1679 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1679, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1679 BINDING SITE, designated SEQ ID:34753, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63539] Another function of VGAM1923 is therefore inhibition of KIAA1679 (Accession XM\_046570). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1679. KIAA1701 (Accession XM\_042087) is another VGAM1923 host target gene. KIAA1701 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1701, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1701 BINDING SITE, designated SEQ ID:33686, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63540] Another function of VGAM1923 is therefore inhibition of KIAA1701 (Accession XM\_042087). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1701. KIAA1750 (Accession XM\_043067) is another VGAM1923 host target gene. KIAA1750 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1750, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1750 BINDING SITE, designated SEQ ID:33878, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63541] Another function of VGAM1923 is therefore inhibition of KIAA1750 (Accession XM\_043067). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1750. KIAA1753 (Accession XM\_036115) is another VGAM1923 host target gene. KIAA1753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1753 BINDING SITE, designated SEQ ID:32381, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63542] Another function of VGAM1923 is therefore inhibition of KIAA1753 (Accession XM\_036115). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1753. LCP (Accession NM\_014315) is another VGAM1923 host target gene. LCP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LCP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LCP BINDING SITE, designated SEQ ID:15615, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63543] Another function of VGAM1923 is therefore inhibition of LCP (Accession NM\_014315). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LCP. LNIR (Accession NM\_030916) is another VGAM1923 host target gene. LNIR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LNIR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LNIR BINDING SITE, designated SEQ ID:25187, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ

ID:4634.

[63544] Another function of VGAM1923 is therefore inhibition of LNIR (Accession NM\_030916). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LNIR. Leucine-rich Repeat Protein, Neuronal 3 (LRRN3, Accession XM\_045261) is another VGAM1923 host target gene. LRRN3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LRRN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRRN3 BINDING SITE, designated SEQ ID:34400, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63545] Another function of VGAM1923 is therefore inhibition of Leucine-rich Repeat Protein, Neuronal 3 (LRRN3, Accession XM\_045261). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRRN3. Mitogen-activated Protein Kinase 11 (MAPK11, Accession NM\_002751) is another VGAM1923 host target gene. MAPK11 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAPK11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK11 BINDING SITE, designated SEQ ID:8629, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63546] Another function of VGAM1923 is therefore inhibition of Mitogen-activated Protein Kinase 11 (MAPK11, Accession NM\_002751). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK11. MASA (Accession XM\_035994) is another VGAM1923 host target gene. MASA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MASA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MASA BINDING SITE, designated SEQ ID:32373, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63547] Another function of VGAM1923 is therefore inhibition of

MASA (Accession XM\_035994). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MASA. MGC26655 (Accession NM\_138290) is another VGAM1923 host target gene. MGC26655 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC26655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC26655 BINDING SITE, designated SEQ ID:28703, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63548] Another function of VGAM1923 is therefore inhibition of MGC26655 (Accession NM\_138290). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC26655. MGC4677 (Accession NM\_052871) is another VGAM1923 host target gene. MGC4677 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4677, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the



complementarity of the nucleotide sequences of MGC4677 BINDING SITE, designated SEQ ID:27453, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63549] Another function of VGAM1923 is therefore inhibition of MGC4677 (Accession NM\_052871). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4677. Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM\_145255) is another VGAM1923 host target gene. MRPL10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL10 BINDING SITE, designated SEQ ID:29770, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63550] Another function of VGAM1923 is therefore inhibition of Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM\_145255). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with MRPL10. MSTP028 (Accession NM\_031954) is another VGAM1923 host target gene. MSTP028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSTP028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSTP028 BINDING SITE, designated SEQ ID:25696, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63551] Another function of VGAM1923 is therefore inhibition of MSTP028 (Accession NM\_031954). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSTP028. Phosphodiesterase 3A, CGMP-inhibited (PDE3A, Accession NM\_000921) is another VGAM1923 host target gene. PDE3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE3A BINDING SITE, designated SEQ

ID:6632, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63552] Another function of VGAM1923 is therefore inhibition of Phosphodiesterase 3A, CGMP-inhibited (PDE3A, Accession NM\_000921). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE3A. Protein Tyrosine Phosphatase, Receptor Type, F Polypeptide (PTPRF), Interacting Protein (liprin), Alpha 4 (PPFIA4, Accession XM\_046751) is another VGAM1923 host target gene. PPFIA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPFIA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPFIA4 BINDING SITE, designated SEQ ID:34821, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63553] Another function of VGAM1923 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, F Polypeptide (PTPRF), Interacting Protein (liprin), Alpha 4 (PPFIA4,

Accession XM\_046751). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPFIA4. PR Domain Containing 12 (PRDM12, Accession NM\_021619) is another VGAM1923 host target gene. PRDM12 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRDM12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM12 BINDING SITE, designated SEQ ID:22254, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63554] Another function of VGAM1923 is therefore inhibition of PR Domain Containing 12 (PRDM12, Accession NM\_021619). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM12. RAB6C, Member RAS Oncogene Family (RAB6C, Accession NM\_032144) is another VGAM1923 host target gene. RAB6C BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAB6C, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB6C BINDING SITE, designated SEQ ID:25834, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63555] Another function of VGAM1923 is therefore inhibition of RAB6C, Member RAS Oncogene Family (RAB6C, Accession NM\_032144). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB6C. Sideroflexin 2 (SFXN2, Accession XM\_058359) is another VGAM1923 host target gene. SFXN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFXN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFXN2 BINDING SITE, designated SEQ ID:36606, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63556] Another function of VGAM1923 is therefore inhibition of Sideroflexin 2 (SFXN2, Accession XM\_058359). Accord-

ingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFXN2. Serum Response Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM\_003131) is another VGAM1923 host target gene. SRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRF BINDING SITE, designated SEQ ID:9104, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63557] Another function of VGAM1923 is therefore inhibition of Serum Response Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM\_003131). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRF. Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM\_037202) is another VGAM1923 host target gene. SS18L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

SS18L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SS18L1 BINDING SITE, designated SEQ ID:32563, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63558] Another function of VGAM1923 is therefore inhibition of Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM\_037202). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SS18L1. START Domain Containing 7 (STARD7, Accession NM\_139267) is another VGAM1923 host target gene. STARD7 BINDING SITE1 and STARD7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by STARD7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STARD7 BINDING SITE1 and STARD7 BINDING SITE2, designated SEQ ID:29262 and SEQ ID:21360 respectively, to the nucleotide sequence of VGAM1923 RNA, herein designated

VGAM RNA, also designated SEQ ID:4634.

[63559] Another function of VGAM1923 is therefore inhibition of START Domain Containing 7 (STARD7, Accession NM\_139267). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STARD7. TUSP (Accession NM\_020245) is another VGAM1923 host target gene. TUSP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUSP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUSP BINDING SITE, designated SEQ ID:21533, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63560] Another function of VGAM1923 is therefore inhibition of TUSP (Accession NM\_020245). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUSP. Williams-Beuren Syndrome Chromosome Region 17 (WBSCR17, Accession XM\_088168) is another VGAM1923 host target gene. WBSCR17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA



encoded by WBSCR17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WBSCR17 BINDING SITE, designated SEQ ID:39548, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63561] Another function of VGAM1923 is therefore inhibition of Williams–Beuren Syndrome Chromosome Region 17 (WBSCR17, Accession XM\_088168). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WBSCR17. Zinc Finger RNA Binding Protein (ZFR, Accession NM\_016107) is another VGAM1923 host target gene. ZFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFR BINDING SITE, designated SEQ ID:18188, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63562] Another function of VGAM1923 is therefore inhibition of

Zinc Finger RNA Binding Protein (ZFR, Accession NM\_016107). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFR. LOC115286 (Accession XM\_055644) is another VGAM1923 host target gene.

LOC115286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115286 BINDING SITE, designated SEQ ID:36315, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63563] Another function of VGAM1923 is therefore inhibition of LOC115286 (Accession XM\_055644). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115286. LOC122830 (Accession XM\_058661) is another VGAM1923 host target gene. LOC122830 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122830, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122830 BINDING SITE, designated SEQ ID:36708, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63564] Another function of VGAM1923 is therefore inhibition of LOC122830 (Accession XM\_058661). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122830. LOC126669 (Accession XM\_060121) is another VGAM1923 host target gene. LOC126669 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126669 BINDING SITE, designated SEQ ID:37158, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63565] Another function of VGAM1923 is therefore inhibition of LOC126669 (Accession XM\_060121). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC126669. LOC130639 (Accession XM\_059464) is another VGAM1923 host target gene. LOC130639 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC130639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130639 BINDING SITE, designated SEQ ID:37002, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63566] Another function of VGAM1923 is therefore inhibition of LOC130639 (Accession XM\_059464). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130639. LOC143888 (Accession XM\_084669) is another VGAM1923 host target gene. LOC143888 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143888, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143888 BINDING SITE, designated SEQ ID:37671, to the nucleotide sequence of VGAM1923 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4634.

[63567] Another function of VGAM1923 is therefore inhibition of LOC143888 (Accession XM\_084669). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143888. LOC145009 (Accession XM\_016472) is another VGAM1923 host target gene. LOC145009 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145009 BINDING SITE, designated SEQ ID:30263, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63568] Another function of VGAM1923 is therefore inhibition of LOC145009 (Accession XM\_016472). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145009. LOC145581 (Accession XM\_085176) is another VGAM1923 host target gene. LOC145581 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145581, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145581 BINDING SITE, designated SEQ ID:37902, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63569] Another function of VGAM1923 is therefore inhibition of LOC145581 (Accession XM\_085176). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145581. LOC145820 (Accession XM\_085246) is another VGAM1923 host target gene. LOC145820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145820 BINDING SITE, designated SEQ ID:37991, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63570] Another function of VGAM1923 is therefore inhibition of LOC145820 (Accession XM\_085246). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC145820. LOC146712 (Accession XM\_097068) is another VGAM1923 host target gene. LOC146712 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146712, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146712 BINDING SITE, designated SEQ ID:40712, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63571] Another function of VGAM1923 is therefore inhibition of LOC146712 (Accession XM\_097068). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146712. LOC147136 (Accession XM\_085716) is another VGAM1923 host target gene. LOC147136 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC147136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147136 BINDING SITE, designated SEQ ID:38306, to

the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63572] Another function of VGAM1923 is therefore inhibition of LOC147136 (Accession XM\_085716). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147136. LOC147976 (Accession XM\_085980) is another VGAM1923 host target gene. LOC147976 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147976 BINDING SITE, designated SEQ ID:38427, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63573] Another function of VGAM1923 is therefore inhibition of LOC147976 (Accession XM\_085980). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147976. LOC149401 (Accession XM\_086511) is another VGAM1923 host target gene. LOC149401 BINDING SITE is HOST TARGET binding site found in the 5' un-



translated region of mRNA encoded by LOC149401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149401 BINDING SITE, designated SEQ ID:38738, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63574] Another function of VGAM1923 is therefore inhibition of LOC149401 (Accession XM\_086511). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149401. LOC149721 (Accession XM\_086649) is another VGAM1923 host target gene. LOC149721 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149721 BINDING SITE, designated SEQ ID:38811, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63575] Another function of VGAM1923 is therefore inhibition of LOC149721 (Accession XM\_086649). Accordingly, utilities

of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149721. LOC151475 (Accession XM\_098063) is another VGAM1923 host target gene. LOC151475 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151475 BINDING SITE, designated SEQ ID:41359, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63576] Another function of VGAM1923 is therefore inhibition of LOC151475 (Accession XM\_098063). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151475. LOC153346 (Accession XM\_098364) is another VGAM1923 host target gene. LOC153346 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC153346 BINDING SITE, designated SEQ ID:41618, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63577] Another function of VGAM1923 is therefore inhibition of LOC153346 (Accession XM\_098364). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153346. LOC153592 (Accession XM\_098396) is another VGAM1923 host target gene. LOC153592 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153592, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153592 BINDING SITE, designated SEQ ID:41649, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63578] Another function of VGAM1923 is therefore inhibition of LOC153592 (Accession XM\_098396). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153592. LOC157922 (Accession XM\_098841) is another VGAM1923 host target gene. LOC157922 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157922 BINDING SITE, designated SEQ ID:41890, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63579] Another function of VGAM1923 is therefore inhibition of LOC157922 (Accession XM\_098841). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157922. LOC158476 (Accession XM\_098955) is another VGAM1923 host target gene. LOC158476 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158476 BINDING SITE, designated SEQ ID:42000, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63580] Another function of VGAM1923 is therefore inhibition of

LOC158476 (Accession XM\_098955). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158476. LOC158709 (Accession XM\_088648) is another VGAM1923 host target gene. LOC158709 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158709 BINDING SITE, designated SEQ ID:39883, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63581] Another function of VGAM1923 is therefore inhibition of LOC158709 (Accession XM\_088648). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158709. LOC160418 (Accession XM\_090286) is another VGAM1923 host target gene. LOC160418 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC160418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC160418 BINDING SITE, designated SEQ ID:39997, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63582] Another function of VGAM1923 is therefore inhibition of LOC160418 (Accession XM\_090286). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160418. LOC196027 (Accession XM\_113633) is another VGAM1923 host target gene. LOC196027 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196027, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196027 BINDING SITE, designated SEQ ID:42306, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63583] Another function of VGAM1923 is therefore inhibition of LOC196027 (Accession XM\_113633). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196027. LOC196955 (Accession XM\_085210) is an-

other VGAM1923 host target gene. LOC196955 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196955 BINDING SITE, designated SEQ ID:37941, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63584] Another function of VGAM1923 is therefore inhibition of LOC196955 (Accession XM\_085210). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196955. LOC199858 (Accession XM\_114040) is another VGAM1923 host target gene. LOC199858 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC199858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199858 BINDING SITE, designated SEQ ID:42646, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63585] Another function of VGAM1923 is therefore inhibition of LOC199858 (Accession XM\_114040). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199858. LOC199957 (Accession XM\_114068) is another VGAM1923 host target gene. LOC199957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199957 BINDING SITE, designated SEQ ID:42676, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63586] Another function of VGAM1923 is therefore inhibition of LOC199957 (Accession XM\_114068). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199957. LOC219722 (Accession XM\_167593) is another VGAM1923 host target gene. LOC219722 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219722, corresponding to a HOST TARGET binding site such as BIND-



ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219722 BINDING SITE, designated SEQ ID:44712, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63587] Another function of VGAM1923 is therefore inhibition of LOC219722 (Accession XM\_167593). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219722. LOC219735 (Accession XM\_167601) is another VGAM1923 host target gene. LOC219735 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219735, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219735 BINDING SITE, designated SEQ ID:44721, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63588] Another function of VGAM1923 is therefore inhibition of LOC219735 (Accession XM\_167601). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC219735. LOC220038 (Accession XM\_166257) is another VGAM1923 host target gene. LOC220038 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220038 BINDING SITE, designated SEQ ID:44080, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63589] Another function of VGAM1923 is therefore inhibition of LOC220038 (Accession XM\_166257). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220038. LOC256087 (Accession XM\_170823) is another VGAM1923 host target gene. LOC256087 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256087, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256087 BINDING SITE, designated SEQ ID:45602, to the nucleotide sequence of VGAM1923 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4634.

[63590] Another function of VGAM1923 is therefore inhibition of LOC256087 (Accession XM\_170823). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256087. LOC51706 (Accession XM\_046746) is another VGAM1923 host target gene. LOC51706 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51706 BINDING SITE, designated SEQ ID:34817, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63591] Another function of VGAM1923 is therefore inhibition of LOC51706 (Accession XM\_046746). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51706. LOC90075 (Accession XM\_028742) is another VGAM1923 host target gene. LOC90075 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90075, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90075 BINDING SITE, designated SEQ ID:30739, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63592] Another function of VGAM1923 is therefore inhibition of LOC90075 (Accession XM\_028742). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90075. LOC91380 (Accession XM\_038134) is another VGAM1923 host target gene. LOC91380 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91380, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91380 BINDING SITE, designated SEQ ID:32757, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63593] Another function of VGAM1923 is therefore inhibition of LOC91380 (Accession XM\_038134). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC91380. LOC91496 (Accession XM\_038788) is another VGAM1923 host target gene. LOC91496 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91496, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91496 BINDING SITE, designated SEQ ID:32918, to the nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63594] Another function of VGAM1923 is therefore inhibition of LOC91496 (Accession XM\_038788). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91496. LOC92912 (Accession XM\_047970) is another VGAM1923 host target gene. LOC92912 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC92912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92912 BINDING SITE, designated SEQ ID:35085, to the

nucleotide sequence of VGAM1923 RNA, herein designated VGAM RNA, also designated SEQ ID:4634.

[63595] Another function of VGAM1923 is therefore inhibition of LOC92912 (Accession XM\_047970). Accordingly, utilities of VGAM1923 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92912. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1924 (VGAM1924) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[63596] VGAM1924 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1924 was detected is described hereinabove with reference to Figs. 1–8.

[63597] VGAM1924 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine Distemper Virus. VGAM1924 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[63598] VGAM1924 gene encodes a VGAM1924 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1924 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1924 precursor RNA is designated SEQ ID:1910, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1910 is located at position 1287 relative to the genome of Canine Distemper Virus.

[63599] VGAM1924 precursor RNA folds onto itself, forming VGAM1924 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[63600] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1924 folded precursor RNA into VGAM1924 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1924 RNA is designated SEQ ID:4635, and is provided hereinbelow with reference to the sequence listing part.

[63601] VGAM1924 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1924 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1924 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[63602] VGAM1924 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1924 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1924 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding



sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1924 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1924 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[63603] The complementary binding of VGAM1924 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1924 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1924 host target RNA into VGAM1924 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[63604] It is appreciated that VGAM1924 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1924 host target genes. The mRNA of each one of this plurality of VGAM1924 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1924 RNA, herein designated VGAM RNA, and which when bound by VGAM1924 RNA causes inhibition of translation of respective one or more VGAM1924 host target proteins.

[63605] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1924 gene, herein designated VGAM GENE, on one or more VGAM1924 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[63606] It is yet further appreciated that a function of VGAM1924 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of viral infection by Canine Distemper Virus. Specific functions, and accordingly utilities, of VGAM1924 correlate with, and may be deduced from, the identity of the host target genes which VGAM1924 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[63607] Nucleotide sequences of the VGAM1924 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1924 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1924 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1924 are further described hereinbelow with reference to Table 1.

[63608] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1924 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1924 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[63609] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1924 gene, herein designated VGAM is inhibition of expression of VGAM1924 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1924 correlate with, and may be deduced from, the identity of the target genes which VGAM1924 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[63610] ATP-binding Cassette, Sub-family D (ALD), Member 3 (ABCD3, Accession NM\_002858) is a VGAM1924 host target gene. ABCD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCD3 BINDING SITE, designated SEQ ID:8754, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63611] A function of VGAM1924 is therefore inhibition of ATP-

binding Cassette, Sub-family D (ALD), Member 3 (ABCD3, Accession NM\_002858), a gene which a probable transporter. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCD3. The function of ABCD3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1775. ATP-binding Cassette, Sub-family D (ALD), Member 4 (ABCD4, Accession NM\_020325) is another VGAM1924 host target gene. ABCD4 BINDING SITE1 through ABCD4 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABCD4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCD4 BINDING SITE1 through ABCD4 BINDING SITE4, designated SEQ ID:21587, SEQ ID:21589, SEQ ID:21582 and SEQ ID:21584 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63612] Another function of VGAM1924 is therefore inhibition of ATP-binding Cassette, Sub-family D (ALD), Member 4

(ABCD4, Accession NM\_020325), a gene which Putative peroxisomal ATP binding cassette transporter. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCD4. The function of ABCD4 has been established by previous studies. The peroxisomal membrane contains several ATP-binding cassette (ABC) transporters, including PMP70 (PXMP1; 170995), ALDP (see OMIM Ref. No. 300100), and ALDR (ALDL1; 601081). All 3 proteins are ABC half-transporters, which dimerize to form an active transporter. See 603076. By searching an EST database for homologs of PMP70 and ALDP, Shani et al. (1997) and Holzinger et al. (1997) identified PXMP1L cDNAs. They respectively designated the gene P70R and PMP69. Shani et al. (1997) reported that the predicted 606-amino acid protein has the structure of an ABC half-transporter and shares 25 to 27% sequence identity with PMP70, ALDR, and ALDP. Antibodies against PXMP1L detected a 73-kD protein on Western blots. Immunofluorescence studies localized the protein to peroxisomes. Northern blot analysis revealed that PXMP1L was expressed as a 2.6-kb mRNA in all tissues examined. Holzinger et al. (1997) and Holzinger et al. (1998) found

transcript variants resulting from alternative splicing and use of alternative polyadenylation sites. Holzinger et al. (1998) reported that the PXMP1L gene contains 19 exons and spans approximately 16 kb.

[63613] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63614] Holzinger, A.; Roscher, A. A.; Landgraf, P.; Lichtner, P.; Kammerer, S. : Genomic organization and chromosomal localization of the human peroxisomal membrane protein-1-like protein (PXMP1-L) gene encoding a peroxisomal ABC transporter. FEBS Lett. 426: 238-242, 1998. ; and

[63615] Shani, N.; Jimenez-Sanchez, G.; Steel, G.; Dean, M.; Valle, D. : Identification of a fourth half ABC transporter in the human peroxisomal membrane. Hum. Molec. Genet. 6: 1925-1931, 1997.

[63616] Further studies establishing the function and utilities of ABCD4 are found in John Hopkins OMIM database record ID 603214, and in cited publications numbered 2432-2434 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Acyl-Coenzyme A Dehydrogenase, Short/branched

Chain (ACADSB, Accession NM\_001609) is another VGAM1924 host target gene. ACADSB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ACADSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACADSB BINDING SITE, designated SEQ ID:7313, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63617] Another function of VGAM1924 is therefore inhibition of Acyl-Coenzyme A Dehydrogenase, Short/branched Chain (ACADSB, Accession NM\_001609). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACADSB. Angiopoietin 1 (ANGPT1, Accession NM\_001146) is another VGAM1924 host target gene. ANGPT1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ANGPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANGPT1 BINDING SITE, designated SEQ ID:6814, to the



nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63618] Another function of VGAM1924 is therefore inhibition of Angiopoietin 1 (ANGPT1, Accession NM\_001146), a gene which binds and activates tie2 receptor by inducing its tyrosine phosphorylation. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANGPT1. The function of ANGPT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM291. Amine Oxidase, Copper Containing 3 (vascular adhesion protein 1) (AOC3, Accession NM\_003734) is another VGAM1924 host target gene. AOC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AOC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AOC3 BINDING SITE, designated SEQ ID:9825, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63619] Another function of VGAM1924 is therefore inhibition of

Amine Oxidase, Copper Containing 3 (vascular adhesion protein 1) (AOC3, Accession NM\_003734), a gene which catalyze the oxidative conversion of amines to aldehydes in the presence of copper and quinone cofactor. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AOC3. The function of AOC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM175. Aldehyde Oxidase 1 (AOX1, Accession NM\_001159) is another VGAM1924 host target gene. AOX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AOX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AOX1 BINDING SITE, designated SEQ ID:6826, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63620] Another function of VGAM1924 is therefore inhibition of Aldehyde Oxidase 1 (AOX1, Accession NM\_001159), a gene which converts an aldehyde in the presence of O<sub>2</sub> and H<sub>2</sub>O to an acid and HOOH. Accordingly, utilities of

VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AOX1. The function of AOX1 has been established by previous studies. Aldehyde oxidase (AO) produces hydrogen peroxide and, under certain conditions, can catalyze the formation of superoxide. By PCR of a human liver library with primers based on conserved regions of rat and fly xanthine dehydrogenase (XDH) proteins, Wright et al. (1993) isolated a cDNA fragment. Using this fragment as a probe, they identified human liver cDNAs encoding a predicted 1,336-amino acid protein. The human protein was 49% identical to rat XDH and contained several characteristic XDH signature sequences. However, both Turner et al. (1995) and Berger et al. (1995) identified the cDNA isolated by Wright et al. (1993) as AO, or AOX1. By Northern blot analysis, Wright et al. (1993) determined that AOX1 was expressed as a 5.1-kb mRNA predominantly in liver. They suggested that a 4.5-kb transcript observed in heart, brain, and kidney arose by use of an alternative polyadenylation site. Since defects in oxygen radical metabolism have been implicated in the pathogenesis of the autosomal dominant form of amyotrophic lateral sclerosis (ALS; 105400), Berger et al. (1995) analyzed other

enzymes involved in oxygen radical metabolism for possible involvement in other forms of ALS. Analysis of a YAC contig revealed that the AOX1 gene is within 280 kb of the D2S116 marker, which is inseparable by recombination from the ALS2 (OMIM Ref. No. 205100) locus. Using in situ hybridization, Berger et al. (1995) found that AOX1 is expressed in the ventral horn of the spinal cord, primarily in the glial cells. Based on the tissue localization, linkage data, and the biochemical role of AOX1 in the free radical pathway, these authors suggested that AOX1 is a candidate gene for ALS2.

[63621] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63622] Berger, R.; Mezey, E.; Clancy, K. P.; Harta, G.; Wright, R. M.; Repine, J. E.; Brown, R. H.; Brownstein, M.; Patterson, D. : Analysis of aldehyde oxidase and xanthine dehydrogenase/oxidase as possible candidate genes for autosomal recessive familial amyotrophic lateral sclerosis. *Somat. Cell Molec. Genet.* 21: 121-131, 1995. ; and

[63623] Turner, N. A.; Doyle, W. A.; Ventom, A. M.; Bray, R. C. : Properties of rabbit liver aldehyde oxidase and the relationship of the enzyme to xanthine oxidase and dehydro-

genase. Europ. J.

[63624] Further studies establishing the function and utilities of AOX1 are found in John Hopkins OMIM database record ID 602841, and in cited publications numbered 1131–113 and 8638 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rho Guanine Nucleotide Exchange Factor (GEF) 7 (ARHGEF7, Accession NM\_003899) is another VGAM1924 host target gene. ARHGEF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF7 BINDING SITE, designated SEQ ID:9983, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63625] Another function of VGAM1924 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 7 (ARHGEF7, Accession NM\_003899), a gene which acts as a rac1 guanine nucleotide exchange factor (gef) and can induce membrane ruffling. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ARHGEF7. The function of ARHGEF7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM297.AS3 (Accession NM\_015928) is another VGAM1924 host target gene. AS3 BINDING SITE1 and AS3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AS3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AS3 BINDING SITE1 and AS3 BINDING SITE2, designated SEQ ID:18049 and SEQ ID:18052 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63626] Another function of VGAM1924 is therefore inhibition of AS3 (Accession NM\_015928), a gene which inhibits cell proliferation. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AS3. The function of AS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM393.BCRP2

(Accession XM\_031102) is another VGAM1924 host target gene. BCRP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCRP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCRP2 BINDING SITE, designated SEQ ID:31275, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63627] Another function of VGAM1924 is therefore inhibition of BCRP2 (Accession XM\_031102). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCRP2. Basic Helix-loop-helix Domain Containing, Class B, 3 (BHLHB3, Accession NM\_030762) is another VGAM1924 host target gene. BHLHB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BHLHB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BHLHB3 BINDING SITE, designated SEQ ID:25044, to the nucleotide sequence of

VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63628] Another function of VGAM1924 is therefore inhibition of Basic Helix–loop–helix Domain Containing, Class B, 3 (BHLHB3, Accession NM\_030762), a gene which represses both basal and activated transcription. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BHLHB3. The function of BHLHB3 has been established by previous studies. By searching EST databases for sequences similar to DEC1, followed by 5–prime and 3–prime RACE with chondrocyte cDNA, Fujimoto et al. (2001) obtained cDNAs encoding human and mouse DEC2. The deduced 482–amino acid human DEC2 protein contains a bHLH domain and an Orange domain that are highly conserved with those of mouse Dec2 and rat Sharp1. DEC2 also has a C–terminal alanine/glycine–rich region not seen in DEC1. Northern blot analysis detected a 3.6–kb DEC2 transcript that was highly expressed in skeletal muscle and brain, moderately expressed in pancreas and heart, expressed at low levels in placenta and lung, and expressed at very low levels in liver and kidney. RT–PCR analysis detected ubiquitous but variable expres–



sion of DEC2. Using yeast 1-hybrid screens and reporter analysis, Garriga-Canut et al. (2001) showed that rat Sharp1 binds to the M1 muscarinic acetylcholine receptor (see OMIM Ref. No. CHRM1; 118510) and acts as a transcriptional repressor of both TATA-containing and TATA-less promoters. Repression occurs either via the bHLH domain or via a C-terminal domain that is sensitive to the histone deacetylase inhibitor trichostatin A.

[63629] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63630] Garriga-Canut, M.; Roopra, A.; Buckley, N. J. : The basic helix-loop-helix protein, SHARP-1, represses transcription by a histone deacetylase-dependent and histone deacetylase-independent mechanism. J. Biol. Chem. 276: 14821-14828, 2001. ; and

[63631] Fujimoto, K.; Shen, M.; Noshiro, M.; Matsubara, K.; Shingu, S.; Honda, K.; Yoshida, E.; Suardita, K.; Matsuda, Y.; Kato, Y. : Molecular cloning and characterization of DEC2, a new memb.

[63632] Further studies establishing the function and utilities of BHLHB3 are found in John Hopkins OMIM database record ID 606200, and in cited publications numbered 902-903

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BLTR2 (Accession NM\_019839) is another VGAM1924 host target gene.

BLTR2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BLTR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLTR2 BINDING SITE, designated SEQ ID:21243, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63633] Another function of VGAM1924 is therefore inhibition of BLTR2 (Accession NM\_019839). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLTR2. BRIP1 (Accession NM\_032043) is another VGAM1924 host target gene. BRIP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BRIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRIP1 BINDING SITE, designated SEQ

ID:25754, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63634] Another function of VGAM1924 is therefore inhibition of BRIP1 (Accession NM\_032043). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRIP1. BTG Family, Member 2 (BTG2, Accession NM\_006763) is another VGAM1924 host target gene. BTG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTG2 BINDING SITE, designated SEQ ID:13625, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63635] Another function of VGAM1924 is therefore inhibition of BTG Family, Member 2 (BTG2, Accession NM\_006763). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTG2. Calnexin (CANX, Accession XM\_113469) is another VGAM1924 host target gene.

CANX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CANX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CANX BINDING SITE, designated SEQ ID:42276, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63636] Another function of VGAM1924 is therefore inhibition of Calnexin (CANX, Accession XM\_113469), a gene which may function as a chaperone in the endoplasmic reticulum, involved in the secretion of proteins from the ER to the outer cellular membrane. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CANX. The function of CANX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM116. Capping Protein (actin filament) Muscle Z-line, Alpha 1 (CAPZA1, Accession XM\_052116) is another VGAM1924 host target gene. CAPZA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPZA1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPZA1 BINDING SITE, designated SEQ ID:35953, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63637] Another function of VGAM1924 is therefore inhibition of Capping Protein (actin filament) Muscle Z-line, Alpha 1 (CAPZA1, Accession XM\_052116), a gene which is alpha 1 subunit of actin filament capping protein; binds actin, has roles in cell motility and actin assembly. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPZA1. The function of CAPZA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM547. Caspase Recruitment Domain Family, Member 4 (CARD4, Accession NM\_006092) is another VGAM1924 host target gene. CARD4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CARD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of CARD4 BINDING SITE, designated SEQ ID:12741, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63638] Another function of VGAM1924 is therefore inhibition of Caspase Recruitment Domain Family, Member 4 (CARD4, Accession NM\_006092), a gene which Activates CASP9 to induce apoptosis, regulates activation of NF-kappaB. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARD4. The function of CARD4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM492. Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM\_005093) is another VGAM1924 host target gene. CBFA2T2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFA2T2 BINDING SITE, designated SEQ ID:11553, to the nucleotide sequence of

VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63639] Another function of VGAM1924 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM\_005093), a gene which is a putative transcription factor. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T2. The function of CBFA2T2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Core-binding Factor, Beta Subunit (CBFB, Accession NM\_022845) is another VGAM1924 host target gene. CBFB BINDING SITE1 and CBFB BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CBFB, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFB BINDING SITE1 and CBFB BINDING SITE2, designated SEQ ID:23148 and SEQ ID:7507 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63640] Another function of VGAM1924 is therefore inhibition of Core-binding Factor, Beta Subunit (CBFB, Accession NM\_022845), a gene which is beta subunit of the transcription factor CBF which causes leukemia. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFB. The function of CBFB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM98. Cadherin 6, Type 2, K-cadherin (fetal kidney) (CDH6, Accession NM\_004932) is another VGAM1924 host target gene. CDH6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH6 BINDING SITE, designated SEQ ID:11376, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63641] Another function of VGAM1924 is therefore inhibition of Cadherin 6, Type 2, K-cadherin (fetal kidney) (CDH6, Accession NM\_004932), a gene which is a calcium depen-



dent cell adhesion protein. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH6. The function of CDH6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60. Centaurin, Delta 1 (CENTD1, Accession NM\_015230) is another VGAM1924 host target gene. CENTD1 BINDING SITE1 and CENTD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CENTD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTD1 BINDING SITE1 and CENTD1 BINDING SITE2, designated SEQ ID:17564 and SEQ ID:29202 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63642] Another function of VGAM1924 is therefore inhibition of Centaurin, Delta 1 (CENTD1, Accession NM\_015230), a gene which is involved in cell signaling/communication. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with CENTD1. The function of CENTD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM445. Chorea Acanthocytosis (CHAC, Accession NM\_033305) is another VGAM1924 host target gene. CHAC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHAC BINDING SITE, designated SEQ ID:27140, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63643] Another function of VGAM1924 is therefore inhibition of Chorea Acanthocytosis (CHAC, Accession NM\_033305), a gene which may regulate the cycling of proteins. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHAC. The function of CHAC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM650. Cysteine Knot Superfamily 1,

BMP Antagonist 1 (CKTSF1B1, Accession NM\_013372) is another VGAM1924 host target gene. CKTSF1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKTSF1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKTSF1B1 BINDING SITE, designated SEQ ID:15024, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63644] Another function of VGAM1924 is therefore inhibition of Cysteine Knot Superfamily 1, BMP Antagonist 1 (CKTSF1B1, Accession NM\_013372), a gene which blocks signaling of bone morphogenetic protein (BMP) . Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKTSF1B1. The function of CKTSF1B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. Ceroid-lipofuscinosis, Neuronal 2, Late Infantile (Jansky-Bielschowsky disease) (CLN2, Accession NM\_000391) is another VGAM1924 host target gene. CLN2 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by CLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN2 BINDING SITE, designated SEQ ID:5966, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63645] Another function of VGAM1924 is therefore inhibition of Ceroid-lipofuscinosis, Neuronal 2, Late Infantile (Jansky-Bielschowsky disease) (CLN2, Accession NM\_000391). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN2. Cystinosis, Nephropathic (CTNS, Accession NM\_004937) is another VGAM1924 host target gene. CTNS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CTNS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTNS BINDING SITE, designated SEQ ID:11384, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4635.

[63646] Another function of VGAM1924 is therefore inhibition of Cystinosis, Nephropathic (CTNS, Accession NM\_004937). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTNS. Cytochrome P450, Subfamily IIB (phenobarbital-inducible), Polypeptide 6 (CYP2B6, Accession NM\_000767) is another VGAM1924 host target gene. CYP2B6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP2B6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP2B6 BINDING SITE, designated SEQ ID:6417, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63647] Another function of VGAM1924 is therefore inhibition of Cytochrome P450, Subfamily IIB (phenobarbital-inducible), Polypeptide 6 (CYP2B6, Accession NM\_000767), a gene which oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics. Accordingly, utilities of VGAM1924 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with CYP2B6. The function of CYP2B6 has been established by previous studies. Thum and Borlak (2000) investigated the gene expression of major human cytochrome P450 genes in various regions of explanted hearts from 6 patients with dilated cardiomyopathy and 1 with transposition of the arterial trunk and 2 samples of normal heart. mRNA for cytochrome 2B6 was predominantly expressed in the right ventricle. A strong correlation between tissue-specific gene expression and enzyme activity was found. Thum and Borlak (2000) concluded that their findings showed that expression of genes for cytochrome P450 monooxygenases and verapamil metabolism are found predominantly in the right side of the heart, and suggested that this observation may explain the lack of efficacy of certain cardioselective drugs. Using a cloned cDNA that codes for a human ortholog of the phenobarbital-inducible cytochrome P450IIB subfamily in rodents, Santisteban et al. (1988) localized the CYP2B gene family to 19cen-q13.3 by Southern blot hybridization to DNA extracted from a panel of human-rodent somatic cell hybrids. Miles et al. (1988) established the chromosomal localization of the CYP2B gene subfam-

ily to be 19q12–q13.2, close to the location of CYP2A (OMIM Ref. No. 123960), by Southern blot analysis of human–rodent somatic cell hybrids.

[63648] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63649] Santisteban, I.; Povey, S.; Shephard, E. A.; Phillips, I. R. : The major phenobarbital–inducible cytochrome P–450 gene subfamily (P450IIB) mapped to the long arm of human chromosome 19. *Ann. Hum. Genet.* 52: 129–135, 1988. ; and

[63650] Thum, T.; Borlak, J. : Gene expression in distinct regions of the heart. *Lancet* 355: 979–983, 2000.

[63651] Further studies establishing the function and utilities of CYP2B6 are found in John Hopkins OMIM database record ID 605059, and in cited publications numbered 4708–470 and 11783 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dystroglycan 1 (dystrophin–associated glycoprotein 1) (DAG1, Accession NM\_004393) is another VGAM1924 host target gene. DAG1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DAG1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAG1 BINDING SITE, designated SEQ ID:10637, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63652] Another function of VGAM1924 is therefore inhibition of Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM\_004393), a gene which may provide linkage between the sarcolemma and extracellular matrix (ECM). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAG1. The function of DAG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1095. Diacylglycerol Kinase, Beta 90kDa (DGKB, Accession XM\_166516) is another VGAM1924 host target gene. DGKB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGKB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-



quences of DGKB BINDING SITE, designated SEQ ID:44451, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63653] Another function of VGAM1924 is therefore inhibition of Diacylglycerol Kinase, Beta 90kDa (DGKB, Accession XM\_166516), a gene which regulates the intracellular concentration of the second messenger diacylglycerol (DAG). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKB. The function of DGKB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM497. Disrupted In Schizophrenia 1 (DISC1, Accession NM\_018662) is another VGAM1924 host target gene. DISC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DISC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DISC1 BINDING SITE, designated SEQ ID:20742, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63654] Another function of VGAM1924 is therefore inhibition of Disrupted In Schizophrenia 1 (DISC1, Accession NM\_018662), a gene which has globular N-terminal domain(s) and a helical C-terminal domain. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DISC1. The function of DISC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.DNA

(cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM\_006892) is another VGAM1924 host target gene. DNMT3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNMT3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT3B BINDING SITE, designated SEQ ID:13766, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63655] Another function of VGAM1924 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B,

Accession NM\_006892), a gene which is required for genome wide de novo methylation. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT3B. The function of DNMT3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM280. Diphtheria Toxin Receptor (heparin-binding epidermal growth factor-like growth factor) (DTR, Accession NM\_001945) is another VGAM1924 host target gene. DTR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DTR BINDING SITE, designated SEQ ID:7660, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63656] Another function of VGAM1924 is therefore inhibition of Diphtheria Toxin Receptor (heparin-binding epidermal growth factor-like growth factor) (DTR, Accession NM\_001945), a gene which may be involved in

macrophage-mediated cellular proliferation. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DTR. The function of DTR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM242.DXS1283E (Accession XM\_047871) is another VGAM1924 host target gene. DXS1283E BINDING SITE1 and DXS1283E BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DXS1283E, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DXS1283E BINDING SITE1 and DXS1283E BINDING SITE2, designated SEQ ID:35066 and SEQ ID:35068 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63657] Another function of VGAM1924 is therefore inhibition of DXS1283E (Accession XM\_047871). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DXS1283E. Dual-specificity tyrosine-(Y)-phosphorylation

Regulated Kinase 1A (DYRK1A, Accession NM\_130436) is another VGAM1924 host target gene. DYRK1A BINDING SITE1 through DYRK1A BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DYRK1A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE1 through DYRK1A BINDING SITE3, designated SEQ ID:28189, SEQ ID:7094 and SEQ ID:7679 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63658] Another function of VGAM1924 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM\_130436), a gene which regulates cell proliferation and may be involved in brain development . Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK1A. The function of DYRK1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42.Endothelin Receptor Type B (EDNRB, Accession

NM\_003991) is another VGAM1924 host target gene. EDNRB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EDNRB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDNRB BINDING SITE, designated SEQ ID:10148, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63659] Another function of VGAM1924 is therefore inhibition of Endothelin Receptor Type B (EDNRB, Accession NM\_003991), a gene which is a non-specific receptor for endothelin 1, 2, and 3. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDNRB. The function of EDNRB has been established by previous studies. The 5-prime region of EDNRB is a complex CpG island giving rise to 4 individual transcripts initiating within the island. Pao et al. (2001) analyzed the relationship between methylation and EDNRB expression in human tissues. The CpG island was unmethylated in normal prostate and bladder tissue, whereas it was methylated in colonic ep-

ithelium; DNA from tumors derived from these tissues was frequently hypermethylated. Analysis of 11 individual CpG sites in the CpG island showed that specific sites with high methylation levels in several tumors and cancer cell lines were also methylated in normal tissues, suggesting that these sites might serve as foci for further de novo methylation. A low methylation level in a small region within the 5-prime region correlated with expression of the 5-prime-most transcript, whereas almost complete methylation 200 to 1000 bp downstream of the transcriptional start site did not block expression of this transcript. Treatment with 5-aza-2-prime-deoxycytidine induced transcriptional activation of all 4 EDNRB transcripts. The authors concluded that there is differential, tissue-dependent methylation at the EDNRB 5-prime region, and that hypermethylation immediately 3-prime to the transcriptional start site does not prevent initiation. They further proposed a spreading mechanism for de novo methylation, starting from particular methylation hotspots. Animal model experiments lend further support to the function of EDNRB. The role of the endothelin-B receptor in vascular homeostasis is controversial because the receptor has both pressor and depressor effects in vivo. Spot-

ting lethal rats carry a naturally occurring deletion in the endothelin-B receptor gene that completely abrogates functional receptor expression. Rats homozygous for this mutation die shortly after birth due to congenital distal intestinal aganglionosis. Genetic rescue of homozygous rats from this developmental defect using a dopamine hydroxylase-EDNRB transgene resulted in ETB-deficient adult rats Gariépy et al. (2000). On a sodium-deficient diet, the rats exhibited a normal arterial blood pressure, but on a high-sodium diet the homozygous sl rats became severely hypertensive. Normal pressure was restored in the salt-fed rats when the epithelial sodium channel was blocked with amiloride. Gariépy et al. (2000) concluded that the rescued sl/sl rats are a novel single-locus genetic model of severe salt-sensitive hypertension. The results suggested that these rats are hypertensive because they lack the normal tonic inhibition of the renal epithelial sodium channel.

[63660] It is appreciated that the abovementioned animal model for EDNRB is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[63661] Full details of the abovementioned studies are described



in the following publications, the disclosure of which are hereby incorporated by reference:

- [63662] Pao, M. M.; Tsutsumi, M.; Liang, G.; Uzvolgyi, E.; Gonzales, F. A.; Jones, P. A. : The endothelin receptor B (EDNRB) promoter displays heterogeneous, site specific methylation patterns in normal and tumor cells. Hum. Molec. Genet. 10: 903–910, 2001. ; and
- [63663] Gariepy, C. E.; Ohuchi, T.; Williams, S. C.; Richardson, J. A.; Yanagisawa, M. : Salt-sensitive hypertension in endothelin-B receptor-deficient rats. J. Clin. Invest. 105: 925–933, 2000.
- [63664] Further studies establishing the function and utilities of EDNRB are found in John Hopkins OMIM database record ID 131244, and in cited publications numbered 4040–4043, 2290, 12215–4053, 2642, 2587–2590, 2280, 2591–260 and 2286 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession NM\_000134) is another VGAM1924 host target gene. FABP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FABP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of FABP2 BINDING SITE, designated SEQ ID:5624, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63665] Another function of VGAM1924 is therefore inhibition of Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession NM\_000134), a gene which may have a role in dietary fat uptake or processing. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FABP2. The function of FABP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM951. Fibulin 5 (FBLN5, Accession NM\_006329) is another VGAM1924 host target gene. FBLN5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBLN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBLN5 BINDING SITE, designated SEQ ID:13023, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA,

also designated SEQ ID:4635.

[63666] Another function of VGAM1924 is therefore inhibition of Fibulin 5 (FBLN5, Accession NM\_006329), a gene which promotes adhesion of endothelial cells through interaction of integrins and the rgd motif. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBLN5. The function of FBLN5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1127.F-box and Leucine-rich Repeat Protein 7 (FBXL7, Accession NM\_012304) is another VGAM1924 host target gene. FBXL7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXL7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXL7 BINDING SITE, designated SEQ ID:14671, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63667] Another function of VGAM1924 is therefore inhibition of F-box and Leucine-rich Repeat Protein 7 (FBXL7, Acces-

sion NM\_012304), a gene which may be involved in phosphorylation-dependent ubiquitination. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXL7. The function of FBXL7 has been established by previous studies. The F box, named after cyclin F (CCNF; 600227), in which it was originally observed, is an approximately 40-amino acid motif that binds SKP1 (OMIM Ref. No. 601434). F-box proteins are components of modular E3 ubiquitin protein ligases called SCFs (SKP1, OMIM Ref. No. 603134, F-box proteins), which function in phosphorylation-dependent ubiquitination. Using a yeast 2-hybrid screen with SKP1 as bait, followed by searching sequence databases, Winston et al. (1999) and Cenciarelli et al. (1999) identified 33 mammalian and 26 human F-box proteins, respectively. These contained C termini with leucine-rich repeats (FBXLs, e.g., SKP2 (OMIM Ref. No. 601436)), WD40 domains (FBXWs, e.g., BTRCP (OMIM Ref. No. 603482)), or no recognizable motifs (FBXOs, e.g., CCNF). Winston et al. (1999) predicted the presence of 12 leucine-rich repeats (LRRs) in FBXL7. RT-PCR analysis detected strong expression in all tissues tested, with highest levels in heart, kidney, liver, and lung.

[63668] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63669] Nagase, T.; Ishikawa, K.; Suyama, M.; Kikuno, R.; Hiro-sawa, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. XII. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro. DNA Res. 5: 355–364, 1998. ; and

[63670] Winston, J. T.; Koepp, D. M.; Zhu, C.; Elledge, S. J.; Harper, J. W. : A family of mammalian F-box proteins. Curr. Biol. 9: 1180–1182, 1999.

[63671] Further studies establishing the function and utilities of FBXL7 are found in John Hopkins OMIM database record ID 605656, and in cited publications numbered 40 and 8278 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FCRH1 (Accession NM\_052938) is another VGAM1924 host target gene. FCRH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FCRH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of FCRH1 BINDING SITE, designated SEQ ID:27500, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63672] Another function of VGAM1924 is therefore inhibition of FCRH1 (Accession NM\_052938). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FCRH1. Frizzled Homolog 8 (Drosophila) (FZD8, Accession NM\_031866) is another VGAM1924 host target gene. FZD8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FZD8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD8 BINDING SITE, designated SEQ ID:25623, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63673] Another function of VGAM1924 is therefore inhibition of Frizzled Homolog 8 (Drosophila) (FZD8, Accession NM\_031866), a gene which may be involved in transduction and intercellular transmission of polarity information during tissue morphogenesis and/or in differentiated tis-

sues. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD8. The function of FZD8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM503.UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 3 (GalNAc-T3) (GALNT3, Accession NM\_004482) is another VGAM1924 host target gene. GALNT3 BINDING SITE1 and GALNT3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GALNT3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT3 BINDING SITE1 and GALNT3 BINDING SITE2, designated SEQ ID:10803 and SEQ ID:10804 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63674] Another function of VGAM1924 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 3 (GalNAc-T3) (GALNT3, Accession NM\_004482), a gene which initiates O-

glycosylation of serine and threonine residues. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT3. The function of GALNT3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1565. Glutamate-ammonia Ligase (glutamine synthase) (GLUL, Accession NM\_002065) is another VGAM1924 host target gene. GLUL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLUL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLUL BINDING SITE, designated SEQ ID:7837, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63675] Another function of VGAM1924 is therefore inhibition of Glutamate-ammonia Ligase (glutamine synthase) (GLUL, Accession NM\_002065), a gene which catalyzes the condensation of glutamate and ammonia to form glutamine. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical condi-



tions associated with GLUL. The function of GLUL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM948. Guanine Nucleotide Binding Protein (G protein), Beta Polypeptide 1 (GNB1, Accession NM\_002074) is another VGAM1924 host target gene. GNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNB1 BINDING SITE, designated SEQ ID:7851, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63676] Another function of VGAM1924 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Beta Polypeptide 1 (GNB1, Accession NM\_002074). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNB1. Glutamate Receptor, Metabotropic 4 (GRM4, Accession NM\_000841) is another VGAM1924 host target gene. GRM4 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by GRM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM4 BINDING SITE, designated SEQ ID:6505, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63677] Another function of VGAM1924 is therefore inhibition of Glutamate Receptor, Metabotropic 4 (GRM4, Accession NM\_000841), a gene which is mediated by a g-protein that inhibits adenylate cyclase activity. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM4. The function of GRM4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1052. Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542) is another VGAM1924 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45223, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63678] Another function of VGAM1924 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. Homeo Box B3 (HOXB3, Accession NM\_002146) is another VGAM1924 host target gene. HOXB3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HOXB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXB3 BINDING SITE, designated SEQ

ID:7922, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63679] Another function of VGAM1924 is therefore inhibition of Homeo Box B3 (HOXB3, Accession NM\_002146). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXB3. Heat Shock 70kDa Protein 8 (HSPA8, Accession NM\_006597) is another VGAM1924 host target gene. HSPA8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPA8 BINDING SITE, designated SEQ ID:13371, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63680] Another function of VGAM1924 is therefore inhibition of Heat Shock 70kDa Protein 8 (HSPA8, Accession NM\_006597), a gene which acts as a chaperone. plays an important role in cells by transiently associating with nascent polypeptides to facilitate correct folding. Accord-

ingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPA8. The function of HSPA8 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM258. Inhibitor of DNA Binding 4, Dominant Negative Helix-loop-helix Protein (ID4, Accession NM\_001546) is another VGAM1924 host target gene. ID4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ID4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ID4 BINDING SITE, designated SEQ ID:7272, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63681] Another function of VGAM1924 is therefore inhibition of Inhibitor of DNA Binding 4, Dominant Negative Helix-loop-helix Protein (ID4, Accession NM\_001546), a gene which negatively regulates cell differentiation. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ID4. The function of ID4 and its association with

various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM931. Interleukin 10 Receptor, Alpha (IL10RA, Accession XM\_006447) is another VGAM1924 host target gene. IL10RA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL10RA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL10RA BINDING SITE, designated SEQ ID:29997, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63682] Another function of VGAM1924 is therefore inhibition of Interleukin 10 Receptor, Alpha (IL10RA, Accession XM\_006447), a gene which is a receptor for il-10. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL10RA. The function of IL10RA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM134. Interleukin 8 (IL8, Accession XM\_170504) is another VGAM1924 host target

gene. IL8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL8 BINDING SITE, designated SEQ ID:45338, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63683] Another function of VGAM1924 is therefore inhibition of Interleukin 8 (IL8, Accession XM\_170504). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL8. inositol(myo)-1(or 4)-monophosphatase 1 (IMPA1, Accession NM\_005536) is another VGAM1924 host target gene. IMPA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IMPA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMPA1 BINDING SITE, designated SEQ ID:12057, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63684] Another function of VGAM1924 is therefore inhibition of inositol(myo)-1(or 4)-monophosphatase 1 (IMPA1, Accession NM\_005536), a gene which is responsible for the provision of inositol required for synthesis of phosphatidylinositol and polyphosphoinositides. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMPA1. The function of IMPA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM134. Inhibin, Beta B (activin AB beta polypeptide) (INHBB, Accession NM\_002193) is another VGAM1924 host target gene. INHBB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INHBB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INHBB BINDING SITE, designated SEQ ID:7949, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63685] Another function of VGAM1924 is therefore inhibition of Inhibin, Beta B (activin AB beta polypeptide) (INHBB, Ac-



cession NM\_002193), a gene which inhibits inhibit the secretion of follitropin by the pituitary gland. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INHBB. The function of INHBB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1465. Jerky Homolog-like (mouse) (JRKL, Accession NM\_003772) is another VGAM1924 host target gene. JRKL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JRKL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JRKL BINDING SITE, designated SEQ ID:9855, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63686] Another function of VGAM1924 is therefore inhibition of Jerky Homolog-like (mouse) (JRKL, Accession NM\_003772), a gene which is a Jerky-related protein and similar to centromere binding protein-B and other nuclear regulators. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with JRKL. The function of JRKL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1546. Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 3 (KCNA3, Accession NM\_002232) is another VGAM1924 host target gene. KCNA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNA3 BINDING SITE, designated SEQ ID:8013, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63687] Another function of VGAM1924 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 3 (KCNA3, Accession NM\_002232). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNA3. Potassium Inwardly-rectifying Channel, Subfamily J, Member 16 (KCNJ16, Accession

NM\_018658) is another VGAM1924 host target gene.

KCNJ16 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KCNJ16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ16 BINDING SITE, designated SEQ ID:20728, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63688] Another function of VGAM1924 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 16 (KCNJ16, Accession NM\_018658). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ16. Kynurenine 3-monooxygenase (kynurenine 3-hydroxylase) (KMO, Accession NM\_003679) is another VGAM1924 host target gene. KMO BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KMO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KMO BINDING SITE, desig-

nated SEQ ID:9782, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63689] Another function of VGAM1924 is therefore inhibition of Kynurenine 3-monooxygenase (kynurenine 3-hydroxylase) (KMO, Accession NM\_003679), a gene which may play a role in encephalic photoreception. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KMO. The function of KMO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM162. Like-glycosyltransferase (LARGE, Accession NM\_004737) is another VGAM1924 host target gene. LARGE BINDING SITE1 and LARGE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LARGE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LARGE BINDING SITE1 and LARGE BINDING SITE2, designated SEQ ID:11130 and SEQ ID:28602 respectively, to the nucleotide sequence of

VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63690] Another function of VGAM1924 is therefore inhibition of Like-glycosyltransferase (LARGE, Accession NM\_004737), a gene which is a member of the N-acetylglucosaminyltransferase family. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LARGE. The function of LARGE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM205. Methyl-CpG Binding Domain Protein 1 (MBD1, Accession NM\_002384) is another VGAM1924 host target gene. MBD1 BINDING SITE1 through MBD1 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MBD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBD1 BINDING SITE1 through MBD1 BINDING SITE4, designated SEQ ID:8202, SEQ ID:17972, SEQ ID:17973 and SEQ ID:17974 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated

VGAM RNA, also designated SEQ ID:4635.

[63691] Another function of VGAM1924 is therefore inhibition of Methyl-CpG Binding Domain Protein 1 (MBD1, Accession NM\_002384), a gene which bind specifically to methylated DNA via a methyl-CpG-binding domain (MBD). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBD1. The function of MBD1 has been established by previous studies. Attempts to understand how DNA methylation prevents transcription have centered on 2 alternative mechanisms: direct interference of site-specific methylation with the binding of essential transcription factors, and indirect interference of promoter-proximal methylation with transcription via a protein that binds to methylated DNA. Methyl-CpG-binding protein-1 (MECP1) binds to a variety of methylated sequences in vitro, provided they contain at least 12 symmetrically methylated CpGs. MECP1 has been detected in crude nuclear extracts. Boyes and Bird (1991) and Levine et al. (1991) presented evidence suggesting that the MECP1 protein is a mediator of repression. Methylation of cytosines within the sequence CpG is essential for mouse development and has been linked to transcriptional sup-

pression in vertebrate systems. Methyl-CpG-binding proteins MECP1 and MECP2 (OMIM Ref. No. 300005) bind preferentially to methylated DNA and can inhibit transcription. The rat Mecp2 gene was cloned by Nan et al. (1993) and its methyl-CpG-binding domain (MBD) defined. By searching DNA sequence databases with the MBD sequence, Cross et al. (1997) identified a human cDNA with potential to encode an MBD-like region. Sequencing of the complete cDNA revealed that the open reading frame also encodes 2 cysteine-rich domains that were found in animal DNA methyltransferases (see OMIM Ref. No. DNMT; 126375) and in the mammalian HRX protein, also known as MLL and ALL-1 (OMIM Ref. No. 159555). They designated the protein PCM1 for 'protein containing MBD.' Expressed in bacteria, it showed specific binding to methylated DNA. PCM1 also repressed transcription in vitro in a methylation-dependent manner. A polyclonal antibody raised against the protein was able to bind the native MECP1 complex from HeLa cells, indicating that PCM1 is a component of mammalian MECP1. Using PCR on a hybrid panel and FISH, Hendrich et al. (1999) mapped the MBD1 gene to chromosome 18q21, 2.1 cM distal to MBD2 (OMIM Ref. No. 603547). They mapped the murine

gene to chromosome 18.

[63692] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63693] Boyes, J.; Bird, A. : DNA methylation inhibits transcription indirectly via a methyl-CpG binding protein. Cell 64: 1123-1134, 1991. ; and

[63694] Levine, A.; Cantoni, G. L.; Razin, A. : Inhibition of promoter activity by methylation: possible involvement of protein mediators. Proc. Nat. Acad. Sci. 88: 6515-6518, 1991.

[63695] Further studies establishing the function and utilities of MBD1 are found in John Hopkins OMIM database record ID 156535, and in cited publications numbered 2224-222 and 12709-12711 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Multiple Endocrine Neoplasia I (MEN1, Accession XM\_167804) is another VGAM1924 host target gene. MEN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MEN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-



quences of MEN1 BINDING SITE, designated SEQ ID:44845, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63696] Another function of VGAM1924 is therefore inhibition of Multiple Endocrine Neoplasia I (MEN1, Accession XM\_167804). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEN1. Myotubular Myopathy 1 (MTM1, Accession NM\_000252) is another VGAM1924 host target gene. MTM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTM1 BINDING SITE, designated SEQ ID:5792, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63697] Another function of VGAM1924 is therefore inhibition of Myotubular Myopathy 1 (MTM1, Accession NM\_000252). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTM1.

5-methyltetrahydrofolate-homocysteine Methyltransferase (MTR, Accession NM\_000254) is another VGAM1924 host target gene. MTR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTR BINDING SITE, designated SEQ ID:5796, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63698] Another function of VGAM1924 is therefore inhibition of 5-methyltetrahydrofolate-homocysteine Methyltransferase (MTR, Accession NM\_000254). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTR. V-myc Myelocytomatosis Viral Related Oncogene, Neuroblastoma Derived (avian) (MYCN, Accession NM\_005378) is another VGAM1924 host target gene. MYCN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of MYCN BINDING SITE, designated SEQ ID:11860, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63699] Another function of VGAM1924 is therefore inhibition of V-myc Myelocytomatosis Viral Related Oncogene, Neuroblastoma Derived (avian) (MYCN, Accession NM\_005378), a gene which may function as a transcription factor. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYCN. The function of MYCN has been established by previous studies. Reiter and Brodeur (1996) generated a high-resolution restriction map of approximately 500 kb spanning the MYCN locus. They found that deletions and rearrangements of the amplicon occurred less often in primary tumors than in cell lines. They also defined a 130-kb common core region of the MYCN amplicon that was amplified in 32 of 33 neuroblastomas. The authors proposed that despite the large size of most MYCN amplicons, the core region that is consistently amplified in neuroblastomas probably contains the MYCN gene and little else. Armstrong and Krystal

(1992) identified NCYM (OMIM Ref. No. 605374) as a gene that overlaps with MYCN; however, it is transcribed from the opposite DNA strand. The 2 genes appear to be coregulated in tumor cell lines. Guo et al. (1999) performed a comprehensive analysis of deletions of 11q in neuroblastomas: 295 sporadic, 15 familial, and 21 tumor-derived cell lines. Loss of heterozygosity (LOH) analysis was performed at 24 microsatellite loci spanning 11q. LOH was observed at multiple 11q loci in 129 of 295 (44%) sporadic neuroblastomas, 5 of 15 (33%) familial neuroblastomas, and 5 of 21 (24%) neuroblastoma cell lines. A single region of 2.1 cM within 11q23.3, flanked by markers D11S1340 and D11S1299, was deleted in all specimens with 11q LOH. Allelic loss at 11q23 was inversely related to MYCN amplification ( $P$  less than 0.001). Within the subset of cases with a single copy of MYCN, 11q LOH was associated with advanced stage disease, unfavorable histopathology, and decreased overall survival probability. However, 11q LOH was not independently prognostic in multivariate analyses. These data were judged to support the hypothesis that a tumor suppressor gene mapping within 11q23.3 is commonly inactivated during the malignant evolution of a large subset of neu-

roblastomas, especially those with unamplified MYCN.

[63700] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63701] Guo, C.; White, P. S.; Weiss, M. J.; Hogarty, M. D.; Thompson, P. M.; Stram, D. O.; Gerbing, R.; Matthay, K. K.; Seeger, R. C.; Brodeur, G. M.; Maris, J. M. : Allelic deletion at 11q23 is common in MYCN single copy neuroblastomas. *Oncogene* 18: 4948–4957, 1999. ; and

[63702] Reiter, J. L.; Brodeur, G. M. : High-resolution mapping of a 130-kb core region of the MYCN amplicon in neuroblastomas. *Genomics* 32: 97–103, 1996.

[63703] Further studies establishing the function and utilities of MYCN are found in John Hopkins OMIM database record ID 164840, and in cited publications numbered 1728–174 and 1814 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myeloid Differentiation Primary Response Gene (88) (MYD88, Accession NM\_002468) is another VGAM1924 host target gene. MYD88 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYD88, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of MYD88 BINDING SITE, designated SEQ ID:8297, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63704] Another function of VGAM1924 is therefore inhibition of Myeloid Differentiation Primary Response Gene (88) (MYD88, Accession NM\_002468), a gene which is involved in the toll-like receptor and il-1 receptor signaling pathway in the innate immune response. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYD88. The function of MYD88 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18. Sialidase 3 (membrane sialidase) (NEU3, Accession NM\_006656) is another VGAM1924 host target gene. NEU3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEU3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEU3 BINDING SITE, designated SEQ

ID:13458, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63705] Another function of VGAM1924 is therefore inhibition of Sialidase 3 (membrane sialidase) (NEU3, Accession NM\_006656). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEU3. Neuralized-like (Drosophila) (NEURL, Accession NM\_004210) is another VGAM1924 host target gene. NEURL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEURL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEURL BINDING SITE, designated SEQ ID:10413, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63706] Another function of VGAM1924 is therefore inhibition of Neuralized-like (Drosophila) (NEURL, Accession NM\_004210). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEURL. Neurogenic Differ-

entiation 1 (NEUROD1, Accession NM\_002500) is another VGAM1924 host target gene. NEUROD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEUROD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEUROD1 BINDING SITE, designated SEQ ID:8324, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63707] Another function of VGAM1924 is therefore inhibition of Neurogenic Differentiation 1 (NEUROD1, Accession NM\_002500), a gene which acts as a differentiation factor during neurogenesis. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEUROD1. The function of NEUROD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM130. Aminopeptidase Puromycin Sensitive (NPEPPS, Accession NM\_006310) is another VGAM1924 host target gene. NPEPPS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA



encoded by NPEPPS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPEPPS BINDING SITE, designated SEQ ID:13001, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63708] Another function of VGAM1924 is therefore inhibition of Aminopeptidase Puromycin Sensitive (NPEPPS, Accession NM\_006310), a gene which is puromycin-sensitive aminopeptidase and has metallopeptidase activity. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPEPPS. The function of NPEPPS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM83. Nuclear Receptor Interacting Protein 1 (NRIP1, Accession XM\_009699) is another VGAM1924 host target gene. NRIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of NRIP1 BINDING SITE, designated SEQ ID:30119, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63709] Another function of VGAM1924 is therefore inhibition of Nuclear Receptor Interacting Protein 1 (NRIP1, Accession XM\_009699), a gene which modulates transcriptional activation by the estrogen receptor. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRIP1. The function of NRIP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM276. Ornithine Aminotransferase (gyrate atrophy) (OAT, Accession NM\_000274) is another VGAM1924 host target gene. OAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAT BINDING SITE, designated SEQ ID:5816, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63710] Another function of VGAM1924 is therefore inhibition of Ornithine Aminotransferase (gyrate atrophy) (OAT, Accession NM\_000274). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAT. Oligophrenin 1 (OPHN1, Accession NM\_002547) is another VGAM1924 host target gene. OPHN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPHN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPHN1 BINDING SITE, designated SEQ ID:8400, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63711] Another function of VGAM1924 is therefore inhibition of Oligophrenin 1 (OPHN1, Accession NM\_002547). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPHN1. Oncostatin M (OSM, Accession NM\_020530) is another VGAM1924 host target gene. OSM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSM, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSM BINDING SITE, designated SEQ ID:21755, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63712] Another function of VGAM1924 is therefore inhibition of Oncostatin M (OSM, Accession NM\_020530), a gene which inhibits the proliferation of a number of tumor cell lines, caused an acute inflammatory reaction. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSM. The function of OSM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1078. Protocadherin Beta 12 (PCDHB12, Accession NM\_018932) is another VGAM1924 host target gene. PCDHB12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHB12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB12 BINDING SITE, designated

SEQ ID:21004, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63713] Another function of VGAM1924 is therefore inhibition of Protocadherin Beta 12 (PCDHB12, Accession NM\_018932). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHB12. Protocadherin Beta 7 (PCDHB7, Accession NM\_018940) is another VGAM1924 host target gene. PCDHB7 BINDING SITE1 and PCDHB7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHB7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB7 BINDING SITE1 and PCDHB7 BINDING SITE2, designated SEQ ID:21006 and SEQ ID:21010 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63714] Another function of VGAM1924 is therefore inhibition of Protocadherin Beta 7 (PCDHB7, Accession NM\_018940). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with PCDHB7. Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM\_003768) is another VGAM1924 host target gene. PEA15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEA15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEA15 BINDING SITE, designated SEQ ID:9847, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63715] Another function of VGAM1924 is therefore inhibition of Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM\_003768), a gene which is a phosphoprotein and involved in glucose uptake. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEA15. The function of PEA15 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM949. Pleckstrin Homology-like Domain, Family A, Member 3 (PHLDA3, Accession NM\_012396) is another VGAM1924 host target gene. PHLDA3 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHLDA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHLDA3 BINDING SITE, designated SEQ ID:14759, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63716] Another function of VGAM1924 is therefore inhibition of Pleckstrin Homology-like Domain, Family A, Member 3 (PHLDA3, Accession NM\_012396). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHLDA3. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM\_014110) is another VGAM1924 host target gene. PPP1R8 BINDING SITE1 through PPP1R8 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PPP1R8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R8 BINDING SITE1 through PPP1R8 BINDING SITE3, designated SEQ ID:15341, SEQ ID:8571

and SEQ ID:28857 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63717] Another function of VGAM1924 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM\_014110), a gene which is an inhibitor subunit of the major nuclear protein phosphatase-1 (pp-1). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R8. The function of PPP1R8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM101. Protein Kinase, CAMP-dependent, Regulatory, Type I, Alpha (tissue specific extinguisher 1) (PRKAR1A, Accession NM\_002734) is another VGAM1924 host target gene. PRKAR1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKAR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAR1A BINDING SITE, designated SEQ ID:8606, to the nucleotide sequence of VGAM1924



RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63718] Another function of VGAM1924 is therefore inhibition of Protein Kinase, CAMP-dependent, Regulatory, Type I, Alpha (tissue specific extinguisher 1) (PRKAR1A, Accession NM\_002734). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAR1A. Phosphoribosyl Pyrophosphate Synthetase 2 (PRPS2, Accession NM\_002765) is another VGAM1924 host target gene. PRPS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPS2 BINDING SITE, designated SEQ ID:8656, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63719] Another function of VGAM1924 is therefore inhibition of Phosphoribosyl Pyrophosphate Synthetase 2 (PRPS2, Accession NM\_002765), a gene which generates the PRPP needed for initiation of purine biosynthesis. Accordingly, utilities of VGAM1924 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with PRPS2. The function of PRPS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM828. PSA (Accession NM\_058179) is another VGAM1924 host target gene. PSA BINDING SITE1 and PSA BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PSA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSA BINDING SITE1 and PSA BINDING SITE2, designated SEQ ID:27739 and SEQ ID:22130 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63720] Another function of VGAM1924 is therefore inhibition of PSA (Accession NM\_058179), a gene which is puromycin-sensitive aminopeptidase and has metallopeptidase activity. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSA. The function of PSA and its association with various diseases and clinical conditions, has been established by previous studies, as described here-

inabove with reference to VGAM65.Phosphotriesterase Related (PTER, Accession NM\_030664) is another VGAM1924 host target gene. PTER BINDING SITE1 and PTER BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTER, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTER BINDING SITE1 and PTER BINDING SITE2, designated SEQ ID:24996 and SEQ ID:24997 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63721] Another function of VGAM1924 is therefore inhibition of Phosphotriesterase Related (PTER, Accession NM\_030664), a gene which is a phosphotriesterase homology protein. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTER. The function of PTER and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM713.Protein Tyrosine Phosphatase, Receptor Type, G (PTPRG, Accession NM\_002841) is another VGAM1924 host target gene. PT-

PRG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTPRG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRG BINDING SITE, designated SEQ ID:8727, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63722] Another function of VGAM1924 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, G (PTPRG, Accession NM\_002841), a gene which is a candidate tumor suppressor and represents a subfamily of receptor tyrosine phosphatases. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRG. The function of PTPRG has been established by previous studies. Changes in the level and pattern of phosphorylation of protein tyrosyl residues are implicated in the control of cellular proliferation. The level of phosphorylation within cells is the result of a balance between the opposing activities of protein-tyrosine kinases and protein-tyrosine phosphatases (PTPs). As more members of the PTP family are cloned, 2 distinct classes have emerged: one class, the

cytoplasmic PTPs, are small soluble proteins; the other class, the receptor PTPs, are large transmembrane proteins. Kaplan et al. (1990) cloned 3 human receptor PTP genes. By analysis of rodent–human somatic cell hybrids retaining overlapping subsets of the entire human genome, LaForgia et al. (1991) mapped the PTPG gene to 3p21–p14. By comparison with other genes mapping to that region, they concluded that PTPG is located in band 3p21 centromeric to the 3p breakpoint in a t(3;8) chromosomal translocation. They showed that 1 PTPG allele was lost in 3 of 5 renal carcinoma cell lines and in 5 of 10 lung carcinoma tumor samples tested. PTPG mRNA was expressed in kidney cell lines and lung cell lines but not in several hematopoietic cell lines tested. Thus the PTPG gene appeared to have characteristics suggesting it as a candidate tumor suppressor gene in renal and lung carcinoma. Latif et al. (1993) localized the PTPRG gene to 3p14.2 by fluorescence in situ hybridization. D3S1249, which represents the PTPRG locus, was localized between D3S1187 and D3S1188 at a recombination fraction of 0.022 and 0.025, respectively, by linkage analysis using the CEPH pedigree panel (Tory et al., 1992). Barnea et al. (1993) cloned cDNAs for the human and mouse PTPRG

gene (symbolized RPTP-gamma by them) from brain cDNA libraries and analyzed their predicted polypeptide sequences. The human (1,445-amino acid) and mouse (1,442-amino acid) sequences share 95% identity at the amino acid level and predict a putative extracellular domain, a single transmembrane domain, and a cytoplasmic region with 2 tandem catalytic tyrosine phosphatase domains. The extracellular domain contains a stretch of 266 amino acids that are highly similar to the zinc-containing enzyme carbonic anhydrase (OMIM Ref. No. 114800), suggesting that RPTP-gamma and RPTP-beta (PTPRZ; 176891) represent a subfamily of receptor tyrosine phosphatases.

[63723] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63724] Barnea, G.; Silvennoinen, O.; Shaanan, B.; Honegger, A. M.; Canoll, P. D.; D'Eustachio, P.; Morse, B.; Levy, J. B.; Laforgia, S.; Huebner, K.; Musacchio, J. M.; Sap, J.; Schlessinger, J. : Identification of a carbonic anhydrase-like domain in the extracellular region of RPTP-gamma defines a new subfamily of receptor tyrosine phosphatases. *Molec. Cell. Biol.* 13: 1497-1506, 1993. ; and

[63725] Latif, F.; Tory, K.; Modi, W.; Geil, L.; LaForgia, S.; Huebner, K.; Zbar, B.; Lerman, M. I. : A MspI polymorphism and linkage mapping of the human protein-tyrosine phosphatase G (PTPRG).

[63726] Further studies establishing the function and utilities of PTPRG are found in John Hopkins OMIM database record ID 176886, and in cited publications numbered 10580, 10890-1058 and 2450 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_002848) is another VGAM1924 host target gene. PTPRO BINDING SITE1 through PTPRO BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRO, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE1 through PTPRO BINDING SITE5, designated SEQ ID:8740, SEQ ID:25005, SEQ ID:25013, SEQ ID:25022 and SEQ ID:25033 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63727] Another function of VGAM1924 is therefore inhibition of

Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM\_002848), a gene which may function as a cell contact receptor that mediates and controls cell-cell signals. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM140.RGL (Accession NM\_015149) is another VGAM1924 host target gene. RGL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGL BINDING SITE, designated SEQ ID:17506, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63728] Another function of VGAM1924 is therefore inhibition of RGL (Accession NM\_015149), a gene which is involved in nucleotide exchange factor. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGL.



The function of RGL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM861. Ribonuclease, RNase A Family, 1 (pancreatic) (RNASE1, Accession XM\_033595) is another VGAM1924 host target gene. RNASE1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RNASE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNASE1 BINDING SITE, designated SEQ ID:31944, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63729] Another function of VGAM1924 is therefore inhibition of Ribonuclease, RNase A Family, 1 (pancreatic) (RNASE1, Accession XM\_033595), a gene which is a Pancreatic ribonuclease; a pyrimidine-specific endonuclease that generates 2',3'-cyclic phosphate products. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNASE1. The function of RNASE1 and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM210. Ring Finger Protein 14 (RNF14, Accession NM\_004290) is another VGAM1924 host target gene. RNF14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF14 BINDING SITE, designated SEQ ID:10504, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63730] Another function of VGAM1924 is therefore inhibition of Ring Finger Protein 14 (RNF14, Accession NM\_004290), a gene which associates with the androgen receptor (AR); functions as a transcriptional coactivator. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF14. The function of RNF14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827. Retinoschisis (X-linked, juvenile) 1 (RS1, Accession NM\_000330) is another VGAM1924

host target gene. RS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RS1 BINDING SITE, designated SEQ ID:5874, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63731] Another function of VGAM1924 is therefore inhibition of Retinoschisis (X-linked, juvenile) 1 (RS1, Accession NM\_000330). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RS1. Reticulon 1 (RTN1, Accession NM\_021136) is another VGAM1924 host target gene. RTN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RTN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RTN1 BINDING SITE, designated SEQ ID:22109, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63732] Another function of VGAM1924 is therefore inhibition of Reticulon 1 (RTN1, Accession NM\_021136), a gene which may be involved in neuroendocrine secretion or in membrane – membrane trafficking in neuroendocrine cells. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RTN1. The function of RTN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM337. Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754) is another VGAM1924 host target gene. RUNX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RUNX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RUNX1 BINDING SITE, designated SEQ ID:7498, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63733] Another function of VGAM1924 is therefore inhibition of Runt-related Transcription Factor 1 (acute myeloid

leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RUNX1. Runt-related Transcription Factor 3 (RUNX3, Accession NM\_004350) is another VGAM1924 host target gene. RUNX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RUNX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RUNX3 BINDING SITE, designated SEQ ID:10549, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63734] Another function of VGAM1924 is therefore inhibition of Runt-related Transcription Factor 3 (RUNX3, Accession NM\_004350), a gene which binds to the core site, 5'-pygpyggt-3', of a number of enhancers and promoters. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RUNX3. The function of RUNX3 and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM1151.SAR1 (Accession NM\_020150) is another VGAM1924 host target gene. SAR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SAR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SAR1 BINDING SITE, designated SEQ ID:21353, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63735] Another function of VGAM1924 is therefore inhibition of SAR1 (Accession NM\_020150), a gene which is involved in transport from the endoplasmic reticulum to the golgi apparatus (by similarity). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAR1. The function of SAR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM222.Syndecan 4 (amphiglycan, ryudocan) (SDC4, Accession NM\_002999) is another VGAM1924 host target gene. SDC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

SDC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC4 BINDING SITE, designated SEQ ID:8893, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63736] Another function of VGAM1924 is therefore inhibition of Syndecan 4 (amphiglycan, ryudocan) (SDC4, Accession NM\_002999), a gene which is a cell surface proteoglycan. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC4. The function of SDC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 13 (SERPINB13, Accession NM\_012397) is another VGAM1924 host target gene. SERPINB13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERPINB13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SER-

PINB13 BINDING SITE, designated SEQ ID:14762, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63737] Another function of VGAM1924 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 13 (SERPINB13, Accession NM\_012397), a gene which plays a role in the proliferation or differentiation of keratinocytes. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERPINB13. The function of SERPINB13 has been established by previous studies. Abts et al. (1999) reported the cloning and characterization of PI13, a novel keratinocyte-associated member of the ovalbumin (ov) family of serpins showing a predominant expression in cells of the human keratinocyte cell line HaCaT and in lesional keratinocytes from psoriatic skin. Initially identified as a UV-repressible gene in HaCaT cells (Abts et al., 1997), this novel serpin is also called 'HaCaT UV-repressible serpin,' or hurpin. Abts et al. (1999) found that the full-length PI13 cDNA encodes a putative 391-amino acid protein with a predicted molecular mass of approximately 44 kD. PI13 shares nearly 59% amino acid identity with SCCA1 (OMIM Ref. No.



600517) and SCCA2 (OMIM Ref. No. 600518). By differential display RT-PCR of oral cavity squamous epithelium, database searching, and screening a keratinocyte cDNA library, Spring et al. (1999) obtained a cDNA encoding PI13, which they termed headpin. Sequence analysis predicted that the 391-amino acid protein contains an inhibitory serpin hinge region, a reactive site loop near the C terminus, and a penultimate serine residue found in all ov-serpin family members. Northern blot analysis detected a 3.3-kb transcript in normal oral mucosa but not in tumor-derived oral mucosa; no expression was detected in any other tissue tested. Relative RT-PCR analysis confirmed low or undetectable expression in squamous carcinoma and head and neck tumor cell lines compared with normal oral mucosa.

[63738] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63739] Abts, H. F.; Welss, T.; Mirmohammadsadegh, A.; Kohrer, K.; Michel, G.; Ruzicka, T. : Cloning and characterization of hurpin (protease inhibitor 13): a new skin-specific, UV-repressible serine proteinase inhibitor of the ovalbumin serpin family. J. Molec. Biol. 293: 29-39, 1999. ; and

[63740] Spring, P.; Nakashima, T.; Frederick, M.; Henderson, Y.; Clayman, G. : Identification and cDNA cloning of headpin, a novel differentially expressed serpin that maps to chromosome 18q. B.

[63741] Further studies establishing the function and utilities of SERPINB13 are found in John Hopkins OMIM database record ID 604445, and in cited publications numbered 1092–1095 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Splicing Factor 1 (SF1, Accession NM\_004630) is another VGAM1924 host target gene. SF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SF1 BINDING SITE, designated SEQ ID:11002, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63742] Another function of VGAM1924 is therefore inhibition of Splicing Factor 1 (SF1, Accession NM\_004630), a gene which is a transcriptional repressor and splicing factor. Accordingly, utilities of VGAM1924 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with SF1. The function of SF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM934. SH3-domain GRB2-like 2 (SH3GL2, Accession NM\_003026) is another VGAM1924 host target gene. SH3GL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3GL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3GL2 BINDING SITE, designated SEQ ID:8968, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63743] Another function of VGAM1924 is therefore inhibition of SH3-domain GRB2-like 2 (SH3GL2, Accession NM\_003026), a gene which plays a role in synaptic vesicle recycling, in particular in clathrin-mediated vesicle endocytosis. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3GL2. The function of SH3GL2 and its association with various diseases and clin-

ical conditions, has been established by previous studies, as described hereinabove with reference to VGAM982.Solute Carrier Family 29 (nucleoside transporters), Member 1 (SLC29A1, Accession NM\_004955) is another VGAM1924 host target gene. SLC29A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC29A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC29A1 BINDING SITE, designated SEQ ID:11398, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63744] Another function of VGAM1924 is therefore inhibition of Solute Carrier Family 29 (nucleoside transporters), Member 1 (SLC29A1, Accession NM\_004955), a gene which mediates both influx and efflux of nucleosides across the membrane. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC29A1. The function of SLC29A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM1908.Small Nuclear Ribonucleoprotein Polypeptide N (SNRPN, Accession NM\_022807) is another VGAM1924 host target gene. SNRPN BINDING SITE1 and SNRPN BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SNRPN, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNRPN BINDING SITE1 and SNRPN BINDING SITE2, designated SEQ ID:23083 and SEQ ID:23085 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63745] Another function of VGAM1924 is therefore inhibition of Small Nuclear Ribonucleoprotein Polypeptide N (SNRPN, Accession NM\_022807), a gene which may be involved in tissue-specific alternative RNA processing events. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNRPN. The function of SNRPN has been established by previous studies. Cattanach et al. (1992) reported observations indicating that maternal duplication of the central part of mouse chromosome 7, where the *Snrpn* gene is located, causes an imprinting effect that

may correspond to PWS. Paternal duplication was not associated with any detectable effect that might correspond with Angelman syndrome (AS; 105830). Mutirangura et al. (1993) constructed a complete YAC contig of the Prader-Willi/Angelman chromosome region and localized the SNRPN gene to specific YACs within the contig. The small nuclear ribonucleoprotein subunit SmN, thought to be involved in splicing of pre-mRNA, is predominantly expressed in brain. The mouse homolog of the SNRPN gene is functionally imprinted in mouse brain, being expressed only from the paternally derived chromosome. Glenn et al. (1993) demonstrated functional imprinting of the human SNRPN gene using RT-PCR. No expression was observed in cultured skin fibroblasts of patients with Prader-Willi syndrome but was found in all patients with Angelman syndrome and in normal controls. Glenn et al. (1993) also demonstrated a parent-specific DNA methylation imprint within intron 5 of the SNRPN gene, which suggested an epigenetic mechanism by which parent-specific expression of this gene might be inherited. Thus, the authors found that the pattern of imprinting fulfills one major criterion for SNRPN being involved in the pathogenesis of PWS. Reed and Leff (1994) characterized a sequence poly-

morphism within expressed portions of the human SNRPN gene and showed that the SNRPN gene is monoallelically expressed in fetal brain and heart and in adult brain.

Analysis of maternal DNA and of SNRPN cDNA confirmed that the maternal allele is not expressed in fetal brain and heart. Thus, maternal imprinting of SNRPN supports the hypothesis that paternal absence of SNRPN is responsible for the PWS phenotype. Kuslich et al. (1999) likewise identified a de novo balanced translocation in a Prader-Willi syndrome patient: (4;15)(q27;q11.2)pat. The breakpoints lay between SNRPN exons 2 and 3. Parental-origin studies indicated that there was no uniparental disomy and no apparent deletion. The patient expressed ZNF127, SNRPN exons 1 and 2, IPW, and PAR1, but did not express either SNRPN exons 3 and 4 or PAR5, as assayed by RT-PCR, of peripheral blood cells. Kuslich et al. (1999) concluded that this patient and that reported by Sun et al. (1996) supported the contention that an intact genomic region and/or transcription of SNRPN exons 2 and 3 play a pivotal role in the manifestations of the major clinical phenotype in PWS. Prader-Willi syndrome and Angelman syndrome are neurogenetic disorders caused by the lack of a paternal or a maternal contribution from human 15q11-q13,

respectively. They involve oppositely imprinted genes: the paternally expressed PWS gene(s) and the maternally expressed AS gene. Deletions in the transcription unit of the imprinted SNRPN gene occur in patients who have PWS or Angelman syndrome because of a parental imprint switch failure in this chromosomal domain. It has been suggested that the SNRPN exon 1 region, which is deleted in PWS patients, contains an imprint switch element from which the maternal and paternal epigenotypes of the 15q11-q13 domain originate. Using the model organism *Drosophila*, Lyko et al. (1998) showed that a fragment from this region can function as a silencer in transgenic flies. Repression was detected specifically from this element and could not be observed with control human sequences. Additional experiments allowed the delineation of the silencer to a fragment of 215 bp containing the SNRPN promoter region. These results provide an additional link between genomic imprinting and an evolutionarily conserved silencing mechanism. Lyko et al. (1998) suggested that the identified element participates in the long-range regulation of the imprinted 15q11-q13 domain or locally represses SNRPN expression from the maternal allele. Animal model experiments lend further sup-



port to the function of SNRPN. Cattanach et al. (1992) reported observations indicating that maternal duplication of the central part of mouse chromosome 7, where the Snrpn gene is located, causes an imprinting effect that may correspond to PWS. Paternal duplication was not associated with any detectable effect that might correspond with Angelman syndrome (AS; 105830).

[63746] It is appreciated that the abovementioned animal model for SNRPN is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[63747] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63748] Wirth, J.; Back, E.; Huttenhofer, A.; Nothwang, H.-G.; Lich, C.; Gross, S.; Menzel, C.; Schinzel, A.; Kioschis, P.; Tommerup, N.; Ropers, H.-H.; Horsthemke, B.; Buiting, K. : A translocation breakpoint cluster disrupts the newly defined 3-prime end of the SNURF-SNRPN transcription unit on chromosome 15. Hum. Molec. Genet. 10: 201-210, 2001. ; and

[63749] Sun, Y.; Nicholls, R. D.; Butler, M. G.; Saitoh, S.; Hainline, B. E.; Palmer, C. G. : Breakage in the SNRPN locus in a bal-

anced 46,XY,t(15;19) Prader-Willi syndrome patient. Hum. Molec. Ge.

[63750] Further studies establishing the function and utilities of SNRPN are found in John Hopkins OMIM database record ID 182279, and in cited publications numbered 1631, 2993-2994, 4204-2998, 48, 2999-3007, 488 and 12400-12405 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sparc/osteonectin, Cwcv and Kazal-like Domains Proteoglycan (testican) (SPOCK, Accession XM\_031696) is another VGAM1924 host target gene. SPOCK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPOCK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPOCK BINDING SITE, designated SEQ ID:31456, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63751] Another function of VGAM1924 is therefore inhibition of Sparc/osteonectin, Cwcv and Kazal-like Domains Proteoglycan (testican) (SPOCK, Accession XM\_031696). Accordingly, utilities of VGAM1924 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with SPOCK. ST3GALVI (Accession NM\_006100) is another VGAM1924 host target gene. ST3GALVI BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ST3GALVI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST3GALVI BINDING SITE, designated SEQ ID:12746, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63752] Another function of VGAM1924 is therefore inhibition of ST3GALVI (Accession NM\_006100), a gene which has a role in synthesis of sialyl-paragloboside. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST3GALVI. The function of ST3GALVI has been established by previous studies. Using mouse St3galv (SIAT9; 604402) as the probe, Okajima et al. (1999) cloned ST3GALVI from a human melanoma cDNA library. The deduced 331-amino acid protein has a calculated molecular mass of about 38 kD. It contains an N-terminal type II transmembrane domain, 2 sialylmotifs, a C-terminal motif

conserved among ST3GAL subfamily members, and 6 potential N-linked glycosylation sites. The ST3GALVI protein shares 38%, 34%, and 33% identity with ST3GALIV, ST3GALIII, and mouse St3galv, respectively. Northern blot analysis revealed abundant expression of 1.8- and 3.0-kb transcripts in heart, placenta, and liver, with lower levels in most other tissues tested. Taniguchi et al. (2001) determined that the ST3GALVI gene contains 10 exons and spans more than 62 kb. They identified 2 unique promoter regions corresponding to 2 mRNA species. The promoters have different constellations of putative transcriptional factor-binding sites, and the type-2 mRNA promoter lacks a canonical TATA box found in the type-1 mRNA promoter.

[63753] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[63754] Okajima, T.; Fukumoto, S.; Miyazaki, H.; Ishida, H.; Kiso, M.; Furukawa, K.; Urano, T.; Furukawa, K. : Molecular cloning of a novel alpha-2,3-sialyltransferase (ST3Gal VI) that sialylates type II lactosamine structures on glycoproteins and glycolipids. J. Biol. Chem. 274: 11479-11486, 1999. ; and

[63755] Taniguchi, A.; Kaneta, R.; Morishita, K.; Matsumoto, K. :  
Gene structure and transcriptional regulation of human  
Gal beta-1,4(3) GlcNac alpha-2,3-sialyltransferase VI  
(hST3Gal VI) gene.

[63756] Further studies establishing the function and utilities of  
ST3GALVI are found in John Hopkins OMIM database  
record ID 607156, and in cited publications numbered  
557 and 5577 listed in the bibliography section hereinbe-  
low, which are also hereby incorporated by refer-  
ence. Signal Transducer and Activator of Transcription 3  
(acute-phase response factor) (STAT3, Accession  
NM\_003150) is another VGAM1924 host target gene.  
STAT3 BINDING SITE1 through STAT3 BINDING SITE4 are  
HOST TARGET binding sites found in untranslated regions  
of mRNA encoded by STAT3, corresponding to HOST TAR-  
GET binding sites such as BINDING SITE I, BINDING SITE II  
or BINDING SITE III. Table 2 illustrates the complementar-  
ity of the nucleotide sequences of STAT3 BINDING SITE1  
through STAT3 BINDING SITE4, designated SEQ ID:9123,  
SEQ ID:9124, SEQ ID:29270 and SEQ ID:29271 respec-  
tively, to the nucleotide sequence of VGAM1924 RNA,  
herein designated VGAM RNA, also designated SEQ  
ID:4635.

[63757] Another function of VGAM1924 is therefore inhibition of Signal Transducer and Activator of Transcription 3 (acute-phase response factor) (STAT3, Accession NM\_003150), a gene which carries out a dual function: signal transduction and activation of transcription. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAT3. The function of STAT3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM329. Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM\_017662) is another VGAM1924 host target gene. TRPM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM6 BINDING SITE, designated SEQ ID:19202, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63758] Another function of VGAM1924 is therefore inhibition of

Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM\_017662), a gene which contains a predicted ion channel domain and a protein kinase domain. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM6. The function of TRPM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173. Translin (TSN, Accession NM\_004622) is another VGAM1924 host target gene. TSN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSN BINDING SITE, designated SEQ ID:10989, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63759] Another function of VGAM1924 is therefore inhibition of Translin (TSN, Accession NM\_004622), a gene which is a DNA binding protein and involved in DNA repair, replication, or recombination. Accordingly, utilities of VGAM1924

include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSN. The function of TSN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM98. Tetratricopeptide Repeat Domain 3 (TTC3, Accession NM\_003316) is another VGAM1924 host target gene. TTC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TTC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTC3 BINDING SITE, designated SEQ ID:9315, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63760] Another function of VGAM1924 is therefore inhibition of Tetratricopeptide Repeat Domain 3 (TTC3, Accession NM\_003316), a gene which contains tetratricopeptide repeat (TPR) motifs. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTC3. The function of TTC3 and its association with various diseases and clinical conditions, has been established by previous studies, as



described hereinabove with reference to VGAM699.UPF3B (Accession NM\_080632) is another VGAM1924 host target gene. UPF3B BINDING SITE1 and UPF3B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UPF3B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UPF3B BINDING SITE1 and UPF3B BINDING SITE2, designated SEQ ID:27935 and SEQ ID:23274 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63761] Another function of VGAM1924 is therefore inhibition of UPF3B (Accession NM\_080632), a gene which facilitates the export of spliced mRNAs and may function as a positive regulator for mannosylphosphate transferase. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UPF3B. The function of UPF3B has been established by previous studies. Lykke-Andersen et al. (2000) found that UPF2, UPF3A, and UPF3B were complexed with UPF1 (RENT1; 601430) while in HeLa cell extracts. In intact cells, UPF3A and UPF3B were found to be

nucleocytoplasmic shuttling proteins, while UPF2 was perinuclear, and UPF1 was cytoplasmic. UPF3A and UPF3B associated selectively with spliced beta-globin (OMIM Ref. No. 141900) mRNA in vivo, and tethering of any UPF protein to the 3-prime untranslated region of beta-globin mRNA elicited NMD. These data suggested that assembly of a dynamic human UPF complex initiates in the nucleus at mRNA exon-exon junctions and triggers NMD in the cytoplasm when recognized downstream of a translation termination site. By immunoprecipitation and immunoblot analyses of nucleoplasmic fractions, Kim et al. (2001) showed that UPF3A and UPF3B are associated in an RNase-resistant manner with Y14 (RBM8A; 605313), as well as with the mRNA export factors ALY (OMIM Ref. No. 604171) and TAP (NXF1; 602647), in mRNA-protein complexes. UPF3 proteins appeared to bind immediately upstream of exon-exon junctions. Kim et al. (2001) concluded that UPF3 proteins facilitate the export of spliced mRNAs by recruiting mRNA export proteins. They proposed that UPF3 functions in NMD and travels with the mRNA to the cytoplasm, where a leading translating ribosome displaces the UPF3-Y14 complexes from the mRNA.

[63762] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [63763] Lykke-Andersen, J.; Shu, M.-D.; Steitz, J. A. : Human Upf proteins target an mRNA for nonsense-mediated decay when bound downstream of a termination codon. Cell 103: 1121-1131, 2000. ; and
- [63764] Kim, V. N.; Kataoka, N.; Dreyfuss, G. : Role of the non-sense-mediated decay factor hUpf3 in the splicing-dependent exon-exon junction complex. Science 293: 1832-1836, 2001.
- [63765] Further studies establishing the function and utilities of UPF3B are found in John Hopkins OMIM database record ID 300298, and in cited publications numbered 9142-9145 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Gamma Polypeptide (YWHAG, Accession NM\_012479) is another VGAM1924 host target gene. YWHAG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YWHAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of YWHAG BINDING SITE, designated SEQ ID:14859, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63766] Another function of VGAM1924 is therefore inhibition of Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Gamma Polypeptide (YWHAG, Accession NM\_012479), a gene which mediates mitogenic signals of PDGF in vascular smooth muscle cells. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YWHAG. The function of YWHAG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Zeta Polypeptide (YWHAZ, Accession NM\_003406) is another VGAM1924 host target gene. YWHAZ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YWHAZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of YWHAZ BINDING SITE, designated SEQ ID:9446, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63767] Another function of VGAM1924 is therefore inhibition of Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Zeta Polypeptide (YWHAZ, Accession NM\_003406), a gene which mediates signal transduction by binding to phosphorylated serine residues on a variety of signaling molecules. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YWHAZ. The function of YWHAZ and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM43. YY1 Transcription Factor (YY1, Accession NM\_003403) is another VGAM1924 host target gene. YY1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YY1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YY1 BINDING SITE, designated SEQ ID:9438, to the nucleotide sequence of VGAM1924 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4635.

[63768] Another function of VGAM1924 is therefore inhibition of YY1 Transcription Factor (YY1, Accession NM\_003403), a gene which is involved in transcriptional regulation and may play an important role in development and differentiation. Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YY1. The function of YY1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1032. Zinc Finger Protein 103 Homolog (mouse) (ZFP103, Accession NM\_005667) is another VGAM1924 host target gene. ZFP103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZFP103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP103 BINDING SITE, designated SEQ ID:12219, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63769] Another function of VGAM1924 is therefore inhibition of

Zinc Finger Protein 103 Homolog (mouse) (ZFP103, Accession NM\_005667). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP103. Zinc Finger Protein 135 (clone pHZ-17) (ZNF135, Accession NM\_003436) is another VGAM1924 host target gene. ZNF135 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF135, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF135 BINDING SITE, designated SEQ ID:9491, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63770] Another function of VGAM1924 is therefore inhibition of Zinc Finger Protein 135 (clone pHZ-17) (ZNF135, Accession NM\_003436). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF135. Zinc Finger Protein 264 (ZNF264, Accession NM\_003417) is another VGAM1924 host target gene. ZNF264 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by ZNF264, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF264 BINDING SITE, designated SEQ ID:9456, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63771] Another function of VGAM1924 is therefore inhibition of Zinc Finger Protein 264 (ZNF264, Accession NM\_003417). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF264. AF311304 (Accession NM\_031214) is another VGAM1924 host target gene. AF311304 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AF311304, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AF311304 BINDING SITE, designated SEQ ID:25261, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63772] Another function of VGAM1924 is therefore inhibition of



AF311304 (Accession NM\_031214). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AF311304. A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248) is another VGAM1924 host target gene. AKAP11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP11 BINDING SITE, designated SEQ ID:18370, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63773] Another function of VGAM1924 is therefore inhibition of A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM\_016248). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP11. A Kinase (PRKA) Anchor Protein 5 (AKAP5, Accession NM\_004857) is another VGAM1924 host target gene. AKAP5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AKAP5, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP5 BINDING SITE, designated SEQ ID:11266, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63774] Another function of VGAM1924 is therefore inhibition of A Kinase (PRKA) Anchor Protein 5 (AKAP5, Accession NM\_004857). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP5. Amyotrophic Lateral Sclerosis 2 (juvenile) Chromosome Region, Candidate 3 (ALS2CR3, Accession NM\_015049) is another VGAM1924 host target gene. ALS2CR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALS2CR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALS2CR3 BINDING SITE, designated SEQ ID:17413, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63775] Another function of VGAM1924 is therefore inhibition of

Amyotrophic Lateral Sclerosis 2 (juvenile) Chromosome Region, Candidate 3 (ALS2CR3, Accession NM\_015049). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALS2CR3. ARAP3 (Accession NM\_022481) is another VGAM1924 host target gene. ARAP3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ARAP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARAP3 BINDING SITE, designated SEQ ID:22855, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63776] Another function of VGAM1924 is therefore inhibition of ARAP3 (Accession NM\_022481). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARAP3. ARTS-1 (Accession NM\_016442) is another VGAM1924 host target gene. ARTS-1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARTS-1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARTS-1 BINDING SITE, designated SEQ ID:18563, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63777] Another function of VGAM1924 is therefore inhibition of ARTS-1 (Accession NM\_016442). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARTS-1. ATPase, (Na<sup>+</sup>)/K<sup>+</sup> Transporting, Beta 4 Polypeptide (ATP1B4, Accession NM\_012069) is another VGAM1924 host target gene. ATP1B4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP1B4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1B4 BINDING SITE, designated SEQ ID:14326, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63778] Another function of VGAM1924 is therefore inhibition of ATPase, (Na<sup>+</sup>)/K<sup>+</sup> Transporting, Beta 4 Polypeptide

(ATP1B4, Accession NM\_012069). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1B4. ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577) is another VGAM1924 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31082, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63779] Another function of VGAM1924 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. BCAA (Accession NM\_016374) is another VGAM1924 host target gene. BCAA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BCAA, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCAA BINDING SITE, designated SEQ ID:18511, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63780] Another function of VGAM1924 is therefore inhibition of BCAA (Accession NM\_016374). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCAA. Basic, Immunoglobulin-like Variable Motif Containing (BIVM, Accession NM\_017693) is another VGAM1924 host target gene. BIVM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BIVM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIVM BINDING SITE, designated SEQ ID:19254, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63781] Another function of VGAM1924 is therefore inhibition of Basic, Immunoglobulin-like Variable Motif Containing (BIVM, Accession NM\_017693). Accordingly, utilities of

VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIVM. BS69 (Accession NM\_006624) is another VGAM1924 host target gene. BS69 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BS69, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BS69 BINDING SITE, designated SEQ ID:13408, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63782] Another function of VGAM1924 is therefore inhibition of BS69 (Accession NM\_006624). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BS69. Chromosome 11 Open Reading Frame 25 (C11orf25, Accession NM\_031418) is another VGAM1924 host target gene. C11orf25 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C11orf25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of C11orf25 BINDING SITE, designated SEQ ID:25403, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63783] Another function of VGAM1924 is therefore inhibition of Chromosome 11 Open Reading Frame 25 (C11orf25, Accession NM\_031418). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf25. Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM\_014837) is another VGAM1924 host target gene. C1orf16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf16 BINDING SITE, designated SEQ ID:16856, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63784] Another function of VGAM1924 is therefore inhibition of Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM\_014837). Accordingly, utilities of VGAM1924 in-



clude diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf16. Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM\_052966) is another VGAM1924 host target gene. C1orf24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf24 BINDING SITE, designated SEQ ID:27530, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63785] Another function of VGAM1924 is therefore inhibition of Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM\_052966). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf24. C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM\_031910) is another VGAM1924 host target gene. C1QTNF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1QTNF6, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QTNF6 BINDING SITE, designated SEQ ID:25659, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63786] Another function of VGAM1924 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM\_031910). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF6. Chromosome 20 Open Reading Frame 142 (C20orf142, Accession XM\_059257) is another VGAM1924 host target gene. C20orf142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf142 BINDING SITE, designated SEQ ID:36933, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63787] Another function of VGAM1924 is therefore inhibition of

Chromosome 20 Open Reading Frame 142 (C20orf142, Accession XM\_059257). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf142. Chromosome 20 Open Reading Frame 36 (C20orf36, Accession NM\_018257) is another VGAM1924 host target gene. C20orf36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf36 BINDING SITE, designated SEQ ID:20224, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63788] Another function of VGAM1924 is therefore inhibition of Chromosome 20 Open Reading Frame 36 (C20orf36, Accession NM\_018257). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf36. Chromosome 20 Open Reading Frame 55 (C20orf55, Accession NM\_031424) is another VGAM1924 host target gene. C20orf55 BINDING SITE is HOST TARGET binding site

found in the 5` untranslated region of mRNA encoded by C20orf55, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf55 BINDING SITE, designated SEQ ID:25407, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63789] Another function of VGAM1924 is therefore inhibition of Chromosome 20 Open Reading Frame 55 (C20orf55, Accession NM\_031424). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf55. Calcium Binding Atopy-related Autoantigen 1 (CBARA1, Accession NM\_006077) is another VGAM1924 host target gene. CBARA1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CBARA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBARA1 BINDING SITE, designated SEQ ID:12722, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ

ID:4635.

[63790] Another function of VGAM1924 is therefore inhibition of Calcium Binding Atopy-related Autoantigen 1 (CBARA1, Accession NM\_006077). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBARA1. Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM\_031409) is another VGAM1924 host target gene. CCR6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CCR6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR6 BINDING SITE, designated SEQ ID:25378, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63791] Another function of VGAM1924 is therefore inhibition of Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM\_031409). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR6. Cat Eye Syndrome Chromosome Region, Candidate 1 (CECR1, Accession NM\_017424) is another VGAM1924 host target gene.

CECR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CECR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CECR1 BINDING SITE, designated SEQ ID:18882, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63792] Another function of VGAM1924 is therefore inhibition of Cat Eye Syndrome Chromosome Region, Candidate 1 (CECR1, Accession NM\_017424). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR1. CGI-127 (Accession NM\_016061) is another VGAM1924 host target gene. CGI-127 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CGI-127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGI-127 BINDING SITE, designated SEQ ID:18137, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4635.

[63793] Another function of VGAM1924 is therefore inhibition of CGI-127 (Accession NM\_016061). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGI-127. CIP29 (Accession NM\_032364) is another VGAM1924 host target gene. CIP29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CIP29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CIP29 BINDING SITE, designated SEQ ID:26149, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63794] Another function of VGAM1924 is therefore inhibition of CIP29 (Accession NM\_032364). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CIP29. Cyclin M4 (CNNM4, Accession NM\_020184) is another VGAM1924 host target gene. CNNM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM4, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNM4 BINDING SITE, designated SEQ ID:21426, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63795] Another function of VGAM1924 is therefore inhibition of Cyclin M4 (CNM4, Accession NM\_020184). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNM4. CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM\_004779) is another VGAM1924 host target gene. CNOT8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT8 BINDING SITE, designated SEQ ID:11182, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63796] Another function of VGAM1924 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 8 (CNOT8,



Accession NM\_004779). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT8. Collectin Sub-family Member 12 (COLEC12, Accession NM\_030781) is another VGAM1924 host target gene. COLEC12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COLEC12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COLEC12 BINDING SITE, designated SEQ ID:25072, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63797] Another function of VGAM1924 is therefore inhibition of Collectin Sub-family Member 12 (COLEC12, Accession NM\_030781). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COLEC12. COP9 Constitutive Photomorphogenic Homolog Subunit 7B (Arabidopsis) (COPS7B, Accession NM\_022730) is another VGAM1924 host target gene. COPS7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by COPS7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COPS7B BINDING SITE, designated SEQ ID:22934, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63798] Another function of VGAM1924 is therefore inhibition of COP9 Constitutive Photomorphogenic Homolog Subunit 7B (Arabidopsis) (COPS7B, Accession NM\_022730). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COPS7B. CCCTC-binding Factor (zinc finger protein) (CTCF, Accession NM\_006565) is another VGAM1924 host target gene. CTCF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTCF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTCF BINDING SITE, designated SEQ ID:13335, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63799] Another function of VGAM1924 is therefore inhibition of CCCTC-binding Factor (zinc finger protein) (CTCF, Accession NM\_006565). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTCF. Chromosome Y Open Reading Frame 15B (CYorf15B, Accession NM\_032576) is another VGAM1924 host target gene. CYorf15B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CYorf15B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYorf15B BINDING SITE, designated SEQ ID:26304, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63800] Another function of VGAM1924 is therefore inhibition of Chromosome Y Open Reading Frame 15B (CYorf15B, Accession NM\_032576). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYorf15B. DDM36 (Accession NM\_020962) is another VGAM1924 host target gene. DDM36 BINDING SITE is HOST TARGET binding site

found in the 3` untranslated region of mRNA encoded by DDM36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDM36 BINDING SITE, designated SEQ ID:21956, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63801] Another function of VGAM1924 is therefore inhibition of DDM36 (Accession NM\_020962). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDM36. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 18 (Myc-regulated) (DDX18, Accession NM\_006773) is another VGAM1924 host target gene. DDX18 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DDX18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX18 BINDING SITE, designated SEQ ID:13646, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63802] Another function of VGAM1924 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 18 (Myc-regulated) (DDX18, Accession NM\_006773). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX18. DiGeorge Syndrome Critical Region Gene 8 (DGCR8, Accession NM\_022720) is another VGAM1924 host target gene. DGCR8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DGCR8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGCR8 BINDING SITE, designated SEQ ID:22920, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63803] Another function of VGAM1924 is therefore inhibition of DiGeorge Syndrome Critical Region Gene 8 (DGCR8, Accession NM\_022720). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGCR8. dj309H15.1 (Accession NM\_138574) is another VGAM1924 host target gene. dj309H15.1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by dj309H15.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of dj309H15.1 BINDING SITE, designated SEQ ID:28888, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63804] Another function of VGAM1924 is therefore inhibition of dj309H15.1 (Accession NM\_138574). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with dj309H15.1. DKFZp434D177 (Accession XM\_086586) is another VGAM1924 host target gene. DKFZp434D177 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp434D177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434D177 BINDING SITE, designated SEQ ID:38779, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63805] Another function of VGAM1924 is therefore inhibition of DKFZp434D177 (Accession XM\_086586). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434D177. DKFZP564B1023 (Accession NM\_031306) is another VGAM1924 host target gene. DKFZP564B1023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564B1023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564B1023 BINDING SITE, designated SEQ ID:25344, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63806] Another function of VGAM1924 is therefore inhibition of DKFZP564B1023 (Accession NM\_031306). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564B1023. DKFZP564I0422 (Accession NM\_031435) is another VGAM1924 host target gene. DKFZP564I0422 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

DKFZP564I0422, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564I0422 BINDING SITE, designated SEQ ID:25437, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63807] Another function of VGAM1924 is therefore inhibition of DKFZP564I0422 (Accession NM\_031435). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I0422. DKFZp566H0824 (Accession NM\_017535) is another VGAM1924 host target gene. DKFZp566H0824 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp566H0824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp566H0824 BINDING SITE, designated SEQ ID:18980, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63808] Another function of VGAM1924 is therefore inhibition of



DKFZp566H0824 (Accession NM\_017535). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp566H0824. DKFZp761D081 (Accession NM\_017610) is another VGAM1924 host target gene. DKFZp761D081 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761D081, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761D081 BINDING SITE, designated SEQ ID:19104, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63809] Another function of VGAM1924 is therefore inhibition of DKFZp761D081 (Accession NM\_017610). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761D081. DKFZp761G0313 (Accession XM\_038026) is another VGAM1924 host target gene. DKFZp761G0313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761G0313, corresponding to a HOST TARGET bind-

ing site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761G0313 BINDING SITE, designated SEQ ID:32741, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63810] Another function of VGAM1924 is therefore inhibition of DKFZp761G0313 (Accession XM\_038026). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761G0313. DKFZp761G2113 (Accession XM\_046017) is another VGAM1924 host target gene. DKFZp761G2113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761G2113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761G2113 BINDING SITE, designated SEQ ID:34643, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63811] Another function of VGAM1924 is therefore inhibition of DKFZp761G2113 (Accession XM\_046017). Accordingly,

utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761G2113. DKFZp761H079 (Accession NM\_144996) is another VGAM1924 host target gene. DKFZp761H079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761H079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761H079 BINDING SITE, designated SEQ ID:29601, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63812] Another function of VGAM1924 is therefore inhibition of DKFZp761H079 (Accession NM\_144996). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761H079. DKFZp762A227 (Accession NM\_017611) is another VGAM1924 host target gene. DKFZp762A227 BINDING SITE1 and DKFZp762A227 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZp762A227, corresponding to HOST TARGET binding sites such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762A227 BINDING SITE1 and DKFZp762A227 BINDING SITE2, designated SEQ ID:19106 and SEQ ID:15318 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63813] Another function of VGAM1924 is therefore inhibition of DKFZp762A227 (Accession NM\_017611). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762A227. ELL2 (Accession NM\_012081) is another VGAM1924 host target gene. ELL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELL2 BINDING SITE, designated SEQ ID:14368, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63814] Another function of VGAM1924 is therefore inhibition of ELL2 (Accession NM\_012081). Accordingly, utilities of

VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELL2. Elongation of Very Long Chain Fatty Acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 2 (ELOVL2, Accession NM\_017770) is another VGAM1924 host target gene. ELOVL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELOVL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELOVL2 BINDING SITE, designated SEQ ID:19390, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63815] Another function of VGAM1924 is therefore inhibition of Elongation of Very Long Chain Fatty Acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 2 (ELOVL2, Accession NM\_017770). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELOVL2. Fibroblast Growth Factor 19 (FGF19, Accession NM\_005117) is another VGAM1924 host target gene. FGF19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF19, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF19 BINDING SITE, designated SEQ ID:11596, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63816] Another function of VGAM1924 is therefore inhibition of Fibroblast Growth Factor 19 (FGF19, Accession NM\_005117). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF19. FHX (Accession NM\_018416) is another VGAM1924 host target gene. FHX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FHX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHX BINDING SITE, designated SEQ ID:20461, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63817] Another function of VGAM1924 is therefore inhibition of FHX (Accession NM\_018416). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FHx. FLJ10246 (Accession NM\_018038) is another VGAM1924 host target gene. FLJ10246 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10246, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10246 BINDING SITE, designated SEQ ID:19786, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63818] Another function of VGAM1924 is therefore inhibition of FLJ10246 (Accession NM\_018038). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10246. FLJ10298 (Accession NM\_018050) is another VGAM1924 host target gene. FLJ10298 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10298, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10298 BINDING SITE, designated SEQ ID:19808, to the nucleotide

sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63819] Another function of VGAM1924 is therefore inhibition of FLJ10298 (Accession NM\_018050). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10298. FLJ10535 (Accession NM\_018129) is another VGAM1924 host target gene. FLJ10535 BINDING SITE1 and FLJ10535 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10535, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10535 BINDING SITE1 and FLJ10535 BINDING SITE2, designated SEQ ID:19918 and SEQ ID:19921 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63820] Another function of VGAM1924 is therefore inhibition of FLJ10535 (Accession NM\_018129). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10535. FLJ10724 (Accession NM\_018194) is another



VGAM1924 host target gene. FLJ10724 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10724, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10724 BINDING SITE, designated SEQ ID:20052, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63821] Another function of VGAM1924 is therefore inhibition of FLJ10724 (Accession NM\_018194). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10724. FLJ10898 (Accession XM\_002486) is another VGAM1924 host target gene. FLJ10898 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10898, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10898 BINDING SITE, designated SEQ ID:29896, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63822] Another function of VGAM1924 is therefore inhibition of FLJ10898 (Accession XM\_002486). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10898. FLJ10961 (Accession XM\_032826) is another VGAM1924 host target gene. FLJ10961 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10961 BINDING SITE, designated SEQ ID:31776, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63823] Another function of VGAM1924 is therefore inhibition of FLJ10961 (Accession XM\_032826). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10961. FLJ11040 (Accession NM\_018307) is another VGAM1924 host target gene. FLJ11040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11040 BINDING SITE, designated SEQ ID:20296, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63824] Another function of VGAM1924 is therefore inhibition of FLJ11040 (Accession NM\_018307). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11040. FLJ11267 (Accession NM\_019607) is another VGAM1924 host target gene. FLJ11267 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11267 BINDING SITE, designated SEQ ID:21226, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63825] Another function of VGAM1924 is therefore inhibition of FLJ11267 (Accession NM\_019607). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ11267. FLJ11275 (Accession NM\_018376) is another VGAM1924 host target gene. FLJ11275 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11275 BINDING SITE, designated SEQ ID:20403, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63826] Another function of VGAM1924 is therefore inhibition of FLJ11275 (Accession NM\_018376). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11275. FLJ11320 (Accession NM\_018389) is another VGAM1924 host target gene. FLJ11320 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11320 BINDING SITE, designated SEQ ID:20426, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM

RNA, also designated SEQ ID:4635.

[63827] Another function of VGAM1924 is therefore inhibition of FLJ11320 (Accession NM\_018389). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11320. FLJ11506 (Accession NM\_024666) is another VGAM1924 host target gene. FLJ11506 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11506 BINDING SITE, designated SEQ ID:23968, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63828] Another function of VGAM1924 is therefore inhibition of FLJ11506 (Accession NM\_024666). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11506. FLJ12619 (Accession NM\_030939) is another VGAM1924 host target gene. FLJ12619 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12619, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12619 BINDING SITE, designated SEQ ID:25209, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63829] Another function of VGAM1924 is therefore inhibition of FLJ12619 (Accession NM\_030939). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12619. FLJ12960 (Accession NM\_024638) is another VGAM1924 host target gene. FLJ12960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12960 BINDING SITE, designated SEQ ID:23914, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63830] Another function of VGAM1924 is therefore inhibition of FLJ12960 (Accession NM\_024638). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ12960. FLJ13188 (Accession NM\_022063) is another VGAM1924 host target gene. FLJ13188 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13188, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13188 BINDING SITE, designated SEQ ID:22606, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63831] Another function of VGAM1924 is therefore inhibition of FLJ13188 (Accession NM\_022063). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13188. FLJ13213 (Accession NM\_024755) is another VGAM1924 host target gene. FLJ13213 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13213 BINDING SITE, designated SEQ ID:24101, to the nucleotide

sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63832] Another function of VGAM1924 is therefore inhibition of FLJ13213 (Accession NM\_024755). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13213. FLJ13614 (Accession NM\_139076) is another VGAM1924 host target gene. FLJ13614 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13614, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13614 BINDING SITE, designated SEQ ID:29152, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63833] Another function of VGAM1924 is therefore inhibition of FLJ13614 (Accession NM\_139076). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13614. FLJ13646 (Accession NM\_024584) is another VGAM1924 host target gene. FLJ13646 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by FLJ13646, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13646 BINDING SITE, designated SEQ ID:23812, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63834] Another function of VGAM1924 is therefore inhibition of FLJ13646 (Accession NM\_024584). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13646. FLJ14054 (Accession NM\_024563) is another VGAM1924 host target gene. FLJ14054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14054 BINDING SITE, designated SEQ ID:23784, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63835] Another function of VGAM1924 is therefore inhibition of FLJ14054 (Accession NM\_024563). Accordingly, utilities of

VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14054. FLJ14100 (Accession NM\_025025) is another VGAM1924 host target gene. FLJ14100 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14100 BINDING SITE, designated SEQ ID:24615, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63836] Another function of VGAM1924 is therefore inhibition of FLJ14100 (Accession NM\_025025). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14100. FLJ14641 (Accession NM\_032817) is another VGAM1924 host target gene. FLJ14641 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14641, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14641

BINDING SITE, designated SEQ ID:26588, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63837] Another function of VGAM1924 is therefore inhibition of FLJ14641 (Accession NM\_032817). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14641. FLJ14803 (Accession NM\_032842) is another VGAM1924 host target gene. FLJ14803 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14803, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14803 BINDING SITE, designated SEQ ID:26629, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63838] Another function of VGAM1924 is therefore inhibition of FLJ14803 (Accession NM\_032842). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14803. FLJ20038 (Accession NM\_017634) is another VGAM1924 host target gene. FLJ20038 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20038 BINDING SITE, designated SEQ ID:19140, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63839] Another function of VGAM1924 is therefore inhibition of FLJ20038 (Accession NM\_017634). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20038. FLJ20051 (Accession NM\_019087) is another VGAM1924 host target gene. FLJ20051 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20051 BINDING SITE, designated SEQ ID:21165, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63840] Another function of VGAM1924 is therefore inhibition of

FLJ20051 (Accession NM\_019087). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20051. FLJ20079 (Accession NM\_017656) is another VGAM1924 host target gene. FLJ20079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19173, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63841] Another function of VGAM1924 is therefore inhibition of FLJ20079 (Accession NM\_017656). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. FLJ20136 (Accession NM\_017684) is another VGAM1924 host target gene. FLJ20136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ20136 BINDING SITE, designated SEQ ID:19230, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63842] Another function of VGAM1924 is therefore inhibition of FLJ20136 (Accession NM\_017684). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20136. FLJ20152 (Accession NM\_019000) is another VGAM1924 host target gene. FLJ20152 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20152 BINDING SITE, designated SEQ ID:21072, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63843] Another function of VGAM1924 is therefore inhibition of FLJ20152 (Accession NM\_019000). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20152. FLJ20277 (Accession NM\_017739) is another

VGAM1924 host target gene. FLJ20277 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20277 BINDING SITE, designated SEQ ID:19330, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63844] Another function of VGAM1924 is therefore inhibition of FLJ20277 (Accession NM\_017739). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20277. FLJ20373 (Accession NM\_017792) is another VGAM1924 host target gene. FLJ20373 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20373 BINDING SITE, designated SEQ ID:19428, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63845] Another function of VGAM1924 is therefore inhibition of FLJ20373 (Accession NM\_017792). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20373. FLJ20396 (Accession NM\_017801) is another VGAM1924 host target gene. FLJ20396 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20396, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20396 BINDING SITE, designated SEQ ID:19446, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63846] Another function of VGAM1924 is therefore inhibition of FLJ20396 (Accession NM\_017801). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20396. FLJ20445 (Accession NM\_017824) is another VGAM1924 host target gene. FLJ20445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20445 BINDING SITE, designated SEQ ID:19478, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63847] Another function of VGAM1924 is therefore inhibition of FLJ20445 (Accession NM\_017824). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20445. FLJ20449 (Accession NM\_017826) is another VGAM1924 host target gene. FLJ20449 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20449 BINDING SITE, designated SEQ ID:19487, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63848] Another function of VGAM1924 is therefore inhibition of FLJ20449 (Accession NM\_017826). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ20449. FLJ21415 (Accession NM\_024738) is another VGAM1924 host target gene. FLJ21415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21415 BINDING SITE, designated SEQ ID:24078, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63849] Another function of VGAM1924 is therefore inhibition of FLJ21415 (Accession NM\_024738). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21415. FLJ22029 (Accession NM\_024949) is another VGAM1924 host target gene. FLJ22029 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22029, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22029 BINDING SITE, designated SEQ ID:24507, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM

RNA, also designated SEQ ID:4635.

[63850] Another function of VGAM1924 is therefore inhibition of FLJ22029 (Accession NM\_024949). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22029. FLJ23151 (Accession NM\_024772) is another VGAM1924 host target gene. FLJ23151 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23151, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23151 BINDING SITE, designated SEQ ID:24137, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63851] Another function of VGAM1924 is therefore inhibition of FLJ23151 (Accession NM\_024772). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23151. FLJ23511 (Accession NM\_032239) is another VGAM1924 host target gene. FLJ23511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23511, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23511 BINDING SITE, designated SEQ ID:25968, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63852] Another function of VGAM1924 is therefore inhibition of FLJ23511 (Accession NM\_032239). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23511. FLJ23563 (Accession XM\_041701) is another VGAM1924 host target gene. FLJ23563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23563 BINDING SITE, designated SEQ ID:33565, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63853] Another function of VGAM1924 is therefore inhibition of FLJ23563 (Accession XM\_041701). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ23563. Far Upstream Element (FUSE) Binding Protein 3 (FUBP3, Accession XM\_033327) is another VGAM1924 host target gene. FUBP3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FUBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUBP3 BINDING SITE, designated SEQ ID:31876, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63854] Another function of VGAM1924 is therefore inhibition of Far Upstream Element (FUSE) Binding Protein 3 (FUBP3, Accession XM\_033327). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUBP3. Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM\_002077) is another VGAM1924 host target gene. GOLGA1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GOLGA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA1 BINDING SITE, designated SEQ ID:7864, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63855] Another function of VGAM1924 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM\_002077). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA1. Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM\_022130) is another VGAM1924 host target gene. GOLPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLPH3 BINDING SITE, designated SEQ ID:22686, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63856] Another function of VGAM1924 is therefore inhibition of Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Acces-

sion NM\_022130). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLPH3. GREB1 (Accession NM\_014668) is another VGAM1924 host target gene. GREB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GREB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GREB1 BINDING SITE, designated SEQ ID:16125, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63857] Another function of VGAM1924 is therefore inhibition of GREB1 (Accession NM\_014668). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GREB1. Glutamate Receptor, Ionotropic, Delta 1 (GRID1, Accession XM\_043613) is another VGAM1924 host target gene. GRID1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRID1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of GRID1 BINDING SITE, designated SEQ ID:33979, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63858] Another function of VGAM1924 is therefore inhibition of Glutamate Receptor, Ionotropic, Delta 1 (GRID1, Accession XM\_043613). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRID1. H2AV (Accession NM\_138635) is another VGAM1924 host target gene. H2AV BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H2AV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H2AV BINDING SITE, designated SEQ ID:28913, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63859] Another function of VGAM1924 is therefore inhibition of H2AV (Accession NM\_138635). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H2AV.



HH114 (Accession NM\_032499) is another VGAM1924 host target gene. HH114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HH114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HH114 BINDING SITE, designated SEQ ID:26250, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63860] Another function of VGAM1924 is therefore inhibition of HH114 (Accession NM\_032499). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HH114. Histamine Receptor H4 (HRH4, Accession NM\_021624) is another VGAM1924 host target gene. HRH4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRH4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRH4 BINDING SITE, designated SEQ ID:22260, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA,

also designated SEQ ID:4635.

[63861] Another function of VGAM1924 is therefore inhibition of Histamine Receptor H4 (HRH4, Accession NM\_021624). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRH4. HSNOV1 (Accession NM\_017515) is another VGAM1924 host target gene. HSNOV1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSNOV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSNOV1 BINDING SITE, designated SEQ ID:18965, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63862] Another function of VGAM1924 is therefore inhibition of HSNOV1 (Accession NM\_017515). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSNOV1. HSPC019 (Accession NM\_014028) is another VGAM1924 host target gene. HSPC019 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by HSPC019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC019 BINDING SITE, designated SEQ ID:15252, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63863] Another function of VGAM1924 is therefore inhibition of HSPC019 (Accession NM\_014028). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC019. IBTK (Accession XM\_041401) is another VGAM1924 host target gene. IBTK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IBTK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IBTK BINDING SITE, designated SEQ ID:33519, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63864] Another function of VGAM1924 is therefore inhibition of IBTK (Accession XM\_041401). Accordingly, utilities of

VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IBTK. Interleukin 14 (IL14, Accession XM\_170924) is another VGAM1924 host target gene. IL14 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by IL14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL14 BINDING SITE, designated SEQ ID:45707, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63865] Another function of VGAM1924 is therefore inhibition of Interleukin 14 (IL14, Accession XM\_170924). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL14. Potassium Voltage-gated Channel, Shal-related Subfamily, Member 1 (KCND1, Accession NM\_004979) is another VGAM1924 host target gene. KCND1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KCND1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of KCND1 BINDING SITE, designated SEQ ID:11428, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63866] Another function of VGAM1924 is therefore inhibition of Potassium Voltage-gated Channel, Shal-related Subfamily, Member 1 (KCND1, Accession NM\_004979). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCND1. KIAA0133 (Accession NM\_014777) is another VGAM1924 host target gene. KIAA0133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0133 BINDING SITE, designated SEQ ID:16611, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63867] Another function of VGAM1924 is therefore inhibition of KIAA0133 (Accession NM\_014777). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0133. KIAA0210 (Accession NM\_014744) is another VGAM1924 host target gene. KIAA0210 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0210 BINDING SITE, designated SEQ ID:16420, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63868] Another function of VGAM1924 is therefore inhibition of KIAA0210 (Accession NM\_014744). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0210. KIAA0218 (Accession NM\_014760) is another VGAM1924 host target gene. KIAA0218 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0218 BINDING SITE, designated SEQ ID:16520, to the nucleotide sequence of VGAM1924 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4635.

[63869] Another function of VGAM1924 is therefore inhibition of KIAA0218 (Accession NM\_014760). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0218. KIAA0232 (Accession XM\_052627) is another VGAM1924 host target gene. KIAA0232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0232 BINDING SITE, designated SEQ ID:36035, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63870] Another function of VGAM1924 is therefore inhibition of KIAA0232 (Accession XM\_052627). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0232. KIAA0252 (Accession XM\_031646) is another VGAM1924 host target gene. KIAA0252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0252, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0252 BINDING SITE, designated SEQ ID:31450, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63871] Another function of VGAM1924 is therefore inhibition of KIAA0252 (Accession XM\_031646). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0252. KIAA0322 (Accession XM\_166591) is another VGAM1924 host target gene. KIAA0322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0322 BINDING SITE, designated SEQ ID:44562, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63872] Another function of VGAM1924 is therefore inhibition of KIAA0322 (Accession XM\_166591). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with KIAA0322. KIAA0332 (Accession XM\_031553) is another VGAM1924 host target gene. KIAA0332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0332 BINDING SITE, designated SEQ ID:31421, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63873] Another function of VGAM1924 is therefore inhibition of KIAA0332 (Accession XM\_031553). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0332. KIAA0408 (Accession NM\_014702) is another VGAM1924 host target gene. KIAA0408 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0408 BINDING SITE, designated SEQ ID:16233, to the

nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63874] Another function of VGAM1924 is therefore inhibition of KIAA0408 (Accession NM\_014702). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0408. KIAA0417 (Accession XM\_048898) is another VGAM1924 host target gene. KIAA0417 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0417, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0417 BINDING SITE, designated SEQ ID:35289, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63875] Another function of VGAM1924 is therefore inhibition of KIAA0417 (Accession XM\_048898). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0417. KIAA0438 (Accession NM\_014819) is another VGAM1924 host target gene. KIAA0438 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0438 BINDING SITE, designated SEQ ID:16786, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63876] Another function of VGAM1924 is therefore inhibition of KIAA0438 (Accession NM\_014819). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0438. KIAA0478 (Accession NM\_014870) is another VGAM1924 host target gene. KIAA0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0478 BINDING SITE, designated SEQ ID:16986, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63877] Another function of VGAM1924 is therefore inhibition of KIAA0478 (Accession NM\_014870). Accordingly, utilities

of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0478. KIAA0493 (Accession XM\_034717) is another VGAM1924 host target gene. KIAA0493 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0493 BINDING SITE, designated SEQ ID:32139, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63878] Another function of VGAM1924 is therefore inhibition of KIAA0493 (Accession XM\_034717). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0493. KIAA0565 (Accession XM\_039912) is another VGAM1924 host target gene. KIAA0565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0565 BINDING SITE, designated SEQ ID:33224, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63879] Another function of VGAM1924 is therefore inhibition of KIAA0565 (Accession XM\_039912). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0565. KIAA0648 (Accession XM\_094043) is another VGAM1924 host target gene. KIAA0648 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0648, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0648 BINDING SITE, designated SEQ ID:40221, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63880] Another function of VGAM1924 is therefore inhibition of KIAA0648 (Accession XM\_094043). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0648. KIAA0663 (Accession NM\_014827) is another VGAM1924 host target gene. KIAA0663 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0663 BINDING SITE, designated SEQ ID:16812, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63881] Another function of VGAM1924 is therefore inhibition of KIAA0663 (Accession NM\_014827). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0663. KIAA0779 (Accession XM\_098229) is another VGAM1924 host target gene. KIAA0779 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0779, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0779 BINDING SITE, designated SEQ ID:41503, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63882] Another function of VGAM1924 is therefore inhibition of

KIAA0779 (Accession XM\_098229). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0779. KIAA0830 (Accession XM\_045759) is another VGAM1924 host target gene. KIAA0830 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0830, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0830 BINDING SITE, designated SEQ ID:34546, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63883] Another function of VGAM1924 is therefore inhibition of KIAA0830 (Accession XM\_045759). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0830. KIAA0854 (Accession NM\_014943) is another VGAM1924 host target gene. KIAA0854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0854 BINDING SITE, designated SEQ ID:17255, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63884] Another function of VGAM1924 is therefore inhibition of KIAA0854 (Accession NM\_014943). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0854. KIAA0865 (Accession XM\_028522) is another VGAM1924 host target gene. KIAA0865 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0865 BINDING SITE, designated SEQ ID:30710, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63885] Another function of VGAM1924 is therefore inhibition of KIAA0865 (Accession XM\_028522). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0865. KIAA0884 (Accession XM\_046660) is another



VGAM1924 host target gene. KIAA0884 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0884, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0884 BINDING SITE, designated SEQ ID:34776, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63886] Another function of VGAM1924 is therefore inhibition of KIAA0884 (Accession XM\_046660). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0884. KIAA0894 (Accession NM\_014896) is another VGAM1924 host target gene. KIAA0894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0894 BINDING SITE, designated SEQ ID:17058, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63887] Another function of VGAM1924 is therefore inhibition of KIAA0894 (Accession NM\_014896). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0894. KIAA0907 (Accession NM\_014949) is another VGAM1924 host target gene. KIAA0907 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0907, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0907 BINDING SITE, designated SEQ ID:17276, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63888] Another function of VGAM1924 is therefore inhibition of KIAA0907 (Accession NM\_014949). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0907. KIAA0979 (Accession NM\_015032) is another VGAM1924 host target gene. KIAA0979 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0979, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0979 BINDING SITE, designated SEQ ID:17386, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63889] Another function of VGAM1924 is therefore inhibition of KIAA0979 (Accession NM\_015032). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0979. KIAA0981 (Accession XM\_028867) is another VGAM1924 host target gene. KIAA0981 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0981 BINDING SITE, designated SEQ ID:30797, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63890] Another function of VGAM1924 is therefore inhibition of KIAA0981 (Accession XM\_028867). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0981. KIAA1025 (Accession XM\_034056) is another VGAM1924 host target gene. KIAA1025 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1025 BINDING SITE, designated SEQ ID:31997, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63891] Another function of VGAM1924 is therefore inhibition of KIAA1025 (Accession XM\_034056). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1025. KIAA1026 (Accession XM\_048825) is another VGAM1924 host target gene. KIAA1026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1026 BINDING SITE, designated SEQ ID:35274, to the nucleotide sequence of VGAM1924 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4635.

[63892] Another function of VGAM1924 is therefore inhibition of KIAA1026 (Accession XM\_048825). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1026. KIAA1055 (Accession XM\_038509) is another VGAM1924 host target gene. KIAA1055 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1055, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1055 BINDING SITE, designated SEQ ID:32850, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63893] Another function of VGAM1924 is therefore inhibition of KIAA1055 (Accession XM\_038509). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1055. KIAA1145 (Accession XM\_037790) is another VGAM1924 host target gene. KIAA1145 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1145, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1145 BINDING SITE, designated SEQ ID:32680, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63894] Another function of VGAM1924 is therefore inhibition of KIAA1145 (Accession XM\_037790). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1145. KIAA1210 (Accession XM\_172801) is another VGAM1924 host target gene. KIAA1210 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1210 BINDING SITE, designated SEQ ID:46088, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63895] Another function of VGAM1924 is therefore inhibition of KIAA1210 (Accession XM\_172801). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1210. KIAA1233 (Accession XM\_032181) is another VGAM1924 host target gene. KIAA1233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1233 BINDING SITE, designated SEQ ID:31593, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63896] Another function of VGAM1924 is therefore inhibition of KIAA1233 (Accession XM\_032181). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1233. KIAA1277 (Accession XM\_035114) is another VGAM1924 host target gene. KIAA1277 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1277 BINDING SITE, designated SEQ ID:32205, to the

nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63897] Another function of VGAM1924 is therefore inhibition of KIAA1277 (Accession XM\_035114). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1277. KIAA1323 (Accession XM\_032146) is another VGAM1924 host target gene. KIAA1323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1323 BINDING SITE, designated SEQ ID:31564, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63898] Another function of VGAM1924 is therefore inhibition of KIAA1323 (Accession XM\_032146). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1323. KIAA1336 (Accession XM\_051306) is another VGAM1924 host target gene. KIAA1336 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by KIAA1336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1336 BINDING SITE, designated SEQ ID:35801, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63899] Another function of VGAM1924 is therefore inhibition of KIAA1336 (Accession XM\_051306). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1336. KIAA1357 (Accession XM\_050421) is another VGAM1924 host target gene. KIAA1357 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1357, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1357 BINDING SITE, designated SEQ ID:35628, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63900] Another function of VGAM1924 is therefore inhibition of KIAA1357 (Accession XM\_050421). Accordingly, utilities

of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1357. KIAA1364 (Accession XM\_032997) is another VGAM1924 host target gene. KIAA1364 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1364, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1364 BINDING SITE, designated SEQ ID:31813, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63901] Another function of VGAM1924 is therefore inhibition of KIAA1364 (Accession XM\_032997). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1364. KIAA1432 (Accession XM\_039698) is another VGAM1924 host target gene. KIAA1432 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1432 BINDING SITE, designated SEQ ID:33153, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63902] Another function of VGAM1924 is therefore inhibition of KIAA1432 (Accession XM\_039698). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1432. KIAA1463 (Accession XM\_051160) is another VGAM1924 host target gene. KIAA1463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1463 BINDING SITE, designated SEQ ID:35775, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63903] Another function of VGAM1924 is therefore inhibition of KIAA1463 (Accession XM\_051160). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1463. KIAA1495 (Accession XM\_055080) is another VGAM1924 host target gene. KIAA1495 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1495 BINDING SITE, designated SEQ ID:36225, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63904] Another function of VGAM1924 is therefore inhibition of KIAA1495 (Accession XM\_055080). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1495. KIAA1505 (Accession XM\_168469) is another VGAM1924 host target gene. KIAA1505 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1505, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1505 BINDING SITE, designated SEQ ID:45194, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63905] Another function of VGAM1924 is therefore inhibition of

KIAA1505 (Accession XM\_168469). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1505. KIAA1509 (Accession XM\_029353) is another VGAM1924 host target gene. KIAA1509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1509 BINDING SITE, designated SEQ ID:30876, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63906] Another function of VGAM1924 is therefore inhibition of KIAA1509 (Accession XM\_029353). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1509. KIAA1594 (Accession XM\_050754) is another VGAM1924 host target gene. KIAA1594 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1594, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1594 BINDING SITE, designated SEQ ID:35674, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63907] Another function of VGAM1924 is therefore inhibition of KIAA1594 (Accession XM\_050754). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1594. KIAA1610 (Accession XM\_040622) is another VGAM1924 host target gene. KIAA1610 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1610, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1610 BINDING SITE, designated SEQ ID:33342, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63908] Another function of VGAM1924 is therefore inhibition of KIAA1610 (Accession XM\_040622). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1610. KIAA1613 (Accession XM\_035946) is another

VGAM1924 host target gene. KIAA1613 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1613, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1613 BINDING SITE, designated SEQ ID:32359, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63909] Another function of VGAM1924 is therefore inhibition of KIAA1613 (Accession XM\_035946). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1613. KIAA1727 (Accession XM\_034262) is another VGAM1924 host target gene. KIAA1727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1727 BINDING SITE, designated SEQ ID:32030, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63910] Another function of VGAM1924 is therefore inhibition of KIAA1727 (Accession XM\_034262). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1727. KIAA1765 (Accession XM\_047355) is another VGAM1924 host target gene. KIAA1765 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1765, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1765 BINDING SITE, designated SEQ ID:34956, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63911] Another function of VGAM1924 is therefore inhibition of KIAA1765 (Accession XM\_047355). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1765. KIAA1822 (Accession XM\_041566) is another VGAM1924 host target gene. KIAA1822 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1822, corresponding to a HOST TARGET binding site such as BINDING SITE I,



BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1822 BINDING SITE, designated SEQ ID:33551, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63912] Another function of VGAM1924 is therefore inhibition of KIAA1822 (Accession XM\_041566). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1822. KIAA1918 (Accession XM\_054951) is another VGAM1924 host target gene. KIAA1918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1918 BINDING SITE, designated SEQ ID:36217, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63913] Another function of VGAM1924 is therefore inhibition of KIAA1918 (Accession XM\_054951). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1918. Keratin, Hair, Basic, 2 (KRTHB2, Accession NM\_033033) is another VGAM1924 host target gene. KRTHB2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KRTHB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KRTHB2 BINDING SITE, designated SEQ ID:26925, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63914] Another function of VGAM1924 is therefore inhibition of Keratin, Hair, Basic, 2 (KRTHB2, Accession NM\_033033). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KRTHB2. LALP1 (Accession NM\_020354) is another VGAM1924 host target gene. LALP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LALP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LALP1 BINDING SITE, designated SEQ

ID:21623, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63915] Another function of VGAM1924 is therefore inhibition of LALP1 (Accession NM\_020354). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LALP1. LIN-28 (Accession NM\_024674) is another VGAM1924 host target gene. LIN-28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIN-28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIN-28 BINDING SITE, designated SEQ ID:23979, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63916] Another function of VGAM1924 is therefore inhibition of LIN-28 (Accession NM\_024674). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIN-28. Leucine Rich Repeat (in FLII) Interacting Protein 1 (LRRFIP1, Accession NM\_004735) is another VGAM1924 host target

gene. LRRFIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRRFIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRRFIP1 BINDING SITE, designated SEQ ID:11121, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63917] Another function of VGAM1924 is therefore inhibition of Leucine Rich Repeat (in FLII) Interacting Protein 1 (LRRFIP1, Accession NM\_004735). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRRFIP1. Mitogen-activated Protein Kinase Kinase 6 (MAP2K6, Accession NM\_002758) is another VGAM1924 host target gene. MAP2K6 BINDING SITE1 and MAP2K6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAP2K6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K6 BINDING SITE1 and MAP2K6 BINDING SITE2,

designated SEQ ID:8643 and SEQ ID:25702 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63918] Another function of VGAM1924 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 6 (MAP2K6, Accession NM\_002758). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K6. Mitogen-activated Protein Kinase Kinase Kinase 3 (MAP4K3, Accession NM\_003618) is another VGAM1924 host target gene. MAP4K3 BINDING SITE1 and MAP4K3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAP4K3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP4K3 BINDING SITE1 and MAP4K3 BINDING SITE2, designated SEQ ID:9683 and SEQ ID:20595 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63919] Another function of VGAM1924 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 3 (MAP4K3, Accession NM\_003618). Accordingly, utilities of

VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP4K3. MGC11034 (Accession NM\_031453) is another VGAM1924 host target gene. MGC11034 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC11034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11034 BINDING SITE, designated SEQ ID:25472, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63920] Another function of VGAM1924 is therefore inhibition of MGC11034 (Accession NM\_031453). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11034. MGC12335 (Accession NM\_032744) is another VGAM1924 host target gene. MGC12335 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC12335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC12335 BINDING SITE, designated SEQ ID:26476, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63921] Another function of VGAM1924 is therefore inhibition of MGC12335 (Accession NM\_032744). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12335. MGC12518 (Accession XM\_034301) is another VGAM1924 host target gene. MGC12518 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12518, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12518 BINDING SITE, designated SEQ ID:32046, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63922] Another function of VGAM1924 is therefore inhibition of MGC12518 (Accession XM\_034301). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12518. MGC13090 (Accession NM\_032711) is another VGAM1924 host target gene. MGC13090 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC13090, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13090 BINDING SITE, designated SEQ ID:26429, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63923] Another function of VGAM1924 is therefore inhibition of MGC13090 (Accession NM\_032711). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13090. MGC13159 (Accession NM\_032927) is another VGAM1924 host target gene. MGC13159 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC13159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13159 BINDING SITE, designated SEQ ID:26752, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63924] Another function of VGAM1924 is therefore inhibition of



MGC13159 (Accession NM\_032927). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13159. MGC13183 (Accession NM\_032358) is another VGAM1924 host target gene. MGC13183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13183 BINDING SITE, designated SEQ ID:26145, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63925] Another function of VGAM1924 is therefore inhibition of MGC13183 (Accession NM\_032358). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13183. MGC14258 (Accession NM\_032900) is another VGAM1924 host target gene. MGC14258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC14258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of MGC14258 BINDING SITE, designated SEQ ID:26723, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63926] Another function of VGAM1924 is therefore inhibition of MGC14258 (Accession NM\_032900). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14258. MGC14433 (Accession NM\_032904) is another VGAM1924 host target gene. MGC14433 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC14433, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14433 BINDING SITE, designated SEQ ID:26726, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63927] Another function of VGAM1924 is therefore inhibition of MGC14433 (Accession NM\_032904). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14433. MGC15437 (Accession NM\_032873) is an-

other VGAM1924 host target gene. MGC15437 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15437 BINDING SITE, designated SEQ ID:26690, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63928] Another function of VGAM1924 is therefore inhibition of MGC15437 (Accession NM\_032873). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15437. MGC2508 (Accession NM\_024327) is another VGAM1924 host target gene. MGC2508 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2508 BINDING SITE, designated SEQ ID:23620, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63929] Another function of VGAM1924 is therefore inhibition of MGC2508 (Accession NM\_024327). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2508. MGC2747 (Accession NM\_024104) is another VGAM1924 host target gene. MGC2747 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2747, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2747 BINDING SITE, designated SEQ ID:23549, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63930] Another function of VGAM1924 is therefore inhibition of MGC2747 (Accession NM\_024104). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2747. MGC4643 (Accession NM\_032715) is another VGAM1924 host target gene. MGC4643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4643, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4643 BINDING SITE, designated SEQ ID:26439, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63931] Another function of VGAM1924 is therefore inhibition of MGC4643 (Accession NM\_032715). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4643. MGC4796 (Accession XM\_029031) is another VGAM1924 host target gene. MGC4796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4796 BINDING SITE, designated SEQ ID:30829, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63932] Another function of VGAM1924 is therefore inhibition of MGC4796 (Accession XM\_029031). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC4796. MGC8721 (Accession XM\_016499) is another VGAM1924 host target gene. MGC8721 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC8721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC8721 BINDING SITE, designated SEQ ID:30267, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63933] Another function of VGAM1924 is therefore inhibition of MGC8721 (Accession XM\_016499). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC8721. Meningioma Expressed Antigen 6 (coiled-coil proline-rich) (MGEA6, Accession NM\_005930) is another VGAM1924 host target gene. MGEA6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGEA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGEA6 BINDING SITE, designated SEQ ID:12562, to the nucleotide se-

quence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63934] Another function of VGAM1924 is therefore inhibition of Meningioma Expressed Antigen 6 (coiled-coil proline-rich) (MGEA6, Accession NM\_005930). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGEA6. MIDORI (Accession XM\_057651) is another VGAM1924 host target gene. MIDORI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIDORI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIDORI BINDING SITE, designated SEQ ID:36528, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63935] Another function of VGAM1924 is therefore inhibition of MIDORI (Accession XM\_057651). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIDORI. Methylenetetrahydrofolate Dehydrogenase (NAD<sup>+</sup> dependent), Methylenetetrahydrofolate Cyclohydrolase

(MTHFD2, Accession NM\_006636) is another VGAM1924 host target gene. MTHFD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MTHFD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTHFD2 BINDING SITE, designated SEQ ID:13431, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63936] Another function of VGAM1924 is therefore inhibition of Methylene Tetrahydrofolate Dehydrogenase (NAD<sup>+</sup> dependent), Methenyltetrahydrofolate Cyclohydrolase (MTHFD2, Accession NM\_006636). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTHFD2. Myelin Transcription Factor 1 (MYT1, Accession NM\_004535) is another VGAM1924 host target gene. MYT1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MYT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-



quences of MYT1 BINDING SITE, designated SEQ ID:10878, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63937] Another function of VGAM1924 is therefore inhibition of Myelin Transcription Factor 1 (MYT1, Accession NM\_004535). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYT1. Nucleosome Assembly Protein 1-like 1 (NAP1L1, Accession NM\_139207) is another VGAM1924 host target gene. NAP1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAP1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAP1L1 BINDING SITE, designated SEQ ID:29225, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63938] Another function of VGAM1924 is therefore inhibition of Nucleosome Assembly Protein 1-like 1 (NAP1L1, Accession NM\_139207). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAP1L1. Ninjurin 2

(NINJ2, Accession NM\_016533) is another VGAM1924 host target gene. NINJ2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NINJ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NINJ2 BINDING SITE, designated SEQ ID:18603, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63939] Another function of VGAM1924 is therefore inhibition of Ninjurin 2 (NINJ2, Accession NM\_016533). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NINJ2. NIP30 (Accession NM\_024946) is another VGAM1924 host target gene. NIP30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NIP30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIP30 BINDING SITE, designated SEQ ID:24498, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4635.

[63940] Another function of VGAM1924 is therefore inhibition of NIP30 (Accession NM\_024946). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIP30. Nudix (nucleoside diphosphate linked moiety X)-type Motif 13 (NUDT13, Accession XM\_032512) is another VGAM1924 host target gene. NUDT13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUDT13 BINDING SITE, designated SEQ ID:31665, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63941] Another function of VGAM1924 is therefore inhibition of Nudix (nucleoside diphosphate linked moiety X)-type Motif 13 (NUDT13, Accession XM\_032512). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUDT13. NY-REN-25 (Accession XM\_027116) is another VGAM1924 host target gene. NY-REN-25 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NY-REN-25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-25 BINDING SITE, designated SEQ ID:30419, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63942] Another function of VGAM1924 is therefore inhibition of NY-REN-25 (Accession XM\_027116). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-25. Ornithine Decarboxylase Antizyme 2 (OAZ2, Accession NM\_002537) is another VGAM1924 host target gene. OAZ2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAZ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAZ2 BINDING SITE, designated SEQ ID:8376, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63943] Another function of VGAM1924 is therefore inhibition of

Ornithine Decarboxylase Antizyme 2 (OAZ2, Accession NM\_002537). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAZ2. Oxysterol Binding Protein-like 11 (OSBPL11, Accession NM\_022776) is another VGAM1924 host target gene. OSBPL11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL11 BINDING SITE, designated SEQ ID:23047, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63944] Another function of VGAM1924 is therefore inhibition of Oxysterol Binding Protein-like 11 (OSBPL11, Accession NM\_022776). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL11. Oxysterol Binding Protein-like 1A (OSBPL1A, Accession NM\_018030) is another VGAM1924 host target gene. OSBPL1A BINDING SITE1 through OSBPL1A BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA en-

coded by OSBPL1A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL1A BINDING SITE1 through OSBPL1A BINDING SITE3, designated SEQ ID:19770, SEQ ID:28422 and SEQ ID:27905 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63945] Another function of VGAM1924 is therefore inhibition of Oxysterol Binding Protein-like 1A (OSBPL1A, Accession NM\_018030). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL1A. PBEF (Accession NM\_005746) is another VGAM1924 host target gene. PBEF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PBEF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PBEF BINDING SITE, designated SEQ ID:12308, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63946] Another function of VGAM1924 is therefore inhibition of

PBEF (Accession NM\_005746). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PBEF. Protocadherin 20 (PCDH20, Accession NM\_022843) is another VGAM1924 host target gene. PCDH20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH20 BINDING SITE, designated SEQ ID:23139, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63947] Another function of VGAM1924 is therefore inhibition of Protocadherin 20 (PCDH20, Accession NM\_022843). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH20. PDZ Domain Containing 2 (PDZD2, Accession XM\_087705) is another VGAM1924 host target gene. PDZD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDZD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDZD2 BINDING SITE, designated SEQ ID:39397, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63948] Another function of VGAM1924 is therefore inhibition of PDZ Domain Containing 2 (PDZD2, Accession XM\_087705). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDZD2. Pellino Homolog 2 (Drosophila) (PELI2, Accession NM\_021255) is another VGAM1924 host target gene. PELI2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PELI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PELI2 BINDING SITE, designated SEQ ID:22229, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63949] Another function of VGAM1924 is therefore inhibition of Pellino Homolog 2 (Drosophila) (PELI2, Accession NM\_021255). Accordingly, utilities of VGAM1924 include



diagnosis, prevention and treatment of diseases and clinical conditions associated with PELI2. Peroxisomal Biogenesis Factor 11B (PEX11B, Accession NM\_003846) is another VGAM1924 host target gene. PEX11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEX11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEX11B BINDING SITE, designated SEQ ID:9944, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63950] Another function of VGAM1924 is therefore inhibition of Peroxisomal Biogenesis Factor 11B (PEX11B, Accession NM\_003846). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEX11B. Phytoceramidase, Alkaline (PHCA, Accession NM\_018367) is another VGAM1924 host target gene. PHCA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of PHCA BINDING SITE, designated SEQ ID:20377, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63951] Another function of VGAM1924 is therefore inhibition of Phytoceramidase, Alkaline (PHCA, Accession NM\_018367). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHCA. PBX/knotted 1 Homeobox 2 (PKNOX2, Accession XM\_165574) is another VGAM1924 host target gene. PKNOX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKNOX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKNOX2 BINDING SITE, designated SEQ ID:43695, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63952] Another function of VGAM1924 is therefore inhibition of PBX/knotted 1 Homeobox 2 (PKNOX2, Accession XM\_165574). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with PKNOX2. Placenta-specific 3 (PLAC3, Accession XM\_045115) is another VGAM1924 host target gene. PLAC3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PLAC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAC3 BINDING SITE, designated SEQ ID:34370, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63953] Another function of VGAM1924 is therefore inhibition of Placenta-specific 3 (PLAC3, Accession XM\_045115). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAC3. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 1B (dopamine and cAMP regulated phosphoprotein, DARPP-32) (PPP1R1B, Accession NM\_032192) is another VGAM1924 host target gene. PPP1R1B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPP1R1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R1B BINDING SITE, designated SEQ ID:25908, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63954] Another function of VGAM1924 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 1B (dopamine and cAMP regulated phosphoprotein, DARPP-32) (PPP1R1B, Accession NM\_032192). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R1B. Protein Phosphatase 2 (formerly 2A), Regulatory Subunit B (PR 52), Alpha Isoform (PPP2R2A, Accession NM\_002717) is another VGAM1924 host target gene. PPP2R2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP2R2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R2A BINDING SITE, designated SEQ ID:8583, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63955] Another function of VGAM1924 is therefore inhibition of Protein Phosphatase 2 (formerly 2A), Regulatory Subunit B (PR 52), Alpha Isoform (PPP2R2A, Accession NM\_002717). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R2A. PRAX-1 (Accession NM\_004758) is another VGAM1924 host target gene. PRAX-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRAX-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRAX-1 BINDING SITE, designated SEQ ID:11147, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63956] Another function of VGAM1924 is therefore inhibition of PRAX-1 (Accession NM\_004758). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRAX-1. PRO1048 (Accession NM\_018497) is another VGAM1924 host target gene. PRO1048 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PRO1048, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1048 BINDING SITE, designated SEQ ID:20564, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63957] Another function of VGAM1924 is therefore inhibition of PRO1048 (Accession NM\_018497). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1048. PRO1617 (Accession NM\_018587) is another VGAM1924 host target gene. PRO1617 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1617 BINDING SITE, designated SEQ ID:20666, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63958] Another function of VGAM1924 is therefore inhibition of PRO1617 (Accession NM\_018587). Accordingly, utilities of

VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1617. Proteasome (prosome, macropain) Inhibitor Subunit 1 (PI31) (PSMF1, Accession NM\_006814) is another VGAM1924 host target gene. PSMF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PSMF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMF1 BINDING SITE, designated SEQ ID:13691, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63959] Another function of VGAM1924 is therefore inhibition of Proteasome (prosome, macropain) Inhibitor Subunit 1 (PI31) (PSMF1, Accession NM\_006814). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMF1. RAB10, Member RAS Oncogene Family (RAB10, Accession XM\_097979) is another VGAM1924 host target gene. RAB10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAB10, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB10 BINDING SITE, designated SEQ ID:41283, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63960] Another function of VGAM1924 is therefore inhibition of RAB10, Member RAS Oncogene Family (RAB10, Accession XM\_097979). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB10. Rab11-FIP2 (Accession NM\_014904) is another VGAM1924 host target gene. Rab11-FIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Rab11-FIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rab11-FIP2 BINDING SITE, designated SEQ ID:17102, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63961] Another function of VGAM1924 is therefore inhibition of Rab11-FIP2 (Accession NM\_014904). Accordingly, utilities



of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rab11-FIP2. RBAK (Accession NM\_021163) is another VGAM1924 host target gene. RBAK BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RBAK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBAK BINDING SITE, designated SEQ ID:22143, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63962] Another function of VGAM1924 is therefore inhibition of RBAK (Accession NM\_021163). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBAK. RI58 (Accession NM\_012420) is another VGAM1924 host target gene. RI58 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RI58, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RI58 BINDING SITE, designated SEQ

ID:14793, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63963] Another function of VGAM1924 is therefore inhibition of RI58 (Accession NM\_012420). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RI58. RMP (Accession NM\_003796) is another VGAM1924 host target gene. RMP BINDING SITE1 and RMP BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RMP, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RMP BINDING SITE1 and RMP BINDING SITE2, designated SEQ ID:9877 and SEQ ID:28680 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63964] Another function of VGAM1924 is therefore inhibition of RMP (Accession NM\_003796). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RMP. Rpo1-2 (Accession NM\_019014) is another VGAM1924

host target gene. Rpo1-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Rpo1-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rpo1-2 BINDING SITE, designated SEQ ID:21099, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63965] Another function of VGAM1924 is therefore inhibition of Rpo1-2 (Accession NM\_019014). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rpo1-2. SCOP (Accession XM\_166290) is another VGAM1924 host target gene. SCOP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCOP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCOP BINDING SITE, designated SEQ ID:44104, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63966] Another function of VGAM1924 is therefore inhibition of SCOP (Accession XM\_166290). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCOP. SCYB11 (Accession XM\_113426) is another VGAM1924 host target gene. SCYB11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SCYB11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYB11 BINDING SITE, designated SEQ ID:42259, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63967] Another function of VGAM1924 is therefore inhibition of SCYB11 (Accession XM\_113426). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCYB11. SDF1 (Accession XM\_165565) is another VGAM1924 host target gene. SDF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SDF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDF1 BINDING SITE, designated SEQ ID:43689, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63968] Another function of VGAM1924 is therefore inhibition of SDF1 (Accession XM\_165565). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDF1. Serine Hydrolase-like (SERHL, Accession XM\_170987) is another VGAM1924 host target gene. SERHL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERHL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERHL BINDING SITE, designated SEQ ID:45757, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63969] Another function of VGAM1924 is therefore inhibition of Serine Hydrolase-like (SERHL, Accession XM\_170987). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with SERHL. Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM\_052832) is another VGAM1924 host target gene. SLC26A7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC26A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A7 BINDING SITE, designated SEQ ID:27413, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63970] Another function of VGAM1924 is therefore inhibition of Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM\_052832). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A7. Sorting Nexin 11 (SNX11, Accession NM\_013323) is another VGAM1924 host target gene. SNX11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNX11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX11 BINDING SITE, des-

ignated SEQ ID:14970, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63971] Another function of VGAM1924 is therefore inhibition of Sorting Nexin 11 (SNX11, Accession NM\_013323). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX11. Spir-1 (Accession XM\_035640) is another VGAM1924 host target gene. Spir-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Spir-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Spir-1 BINDING SITE, designated SEQ ID:32306, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63972] Another function of VGAM1924 is therefore inhibition of Spir-1 (Accession XM\_035640). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Spir-1. Synaptopodin 2 (SYNPO2, Accession XM\_050219) is another VGAM1924 host target gene. SYNPO2 BINDING SITE

is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SYNPO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNPO2 BINDING SITE, designated SEQ ID:35594, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63973] Another function of VGAM1924 is therefore inhibition of Synaptopodin 2 (SYNPO2, Accession XM\_050219). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNPO2. Synaptotagmin-like 4 (granuphilin-a) (SYTL4, Accession NM\_080737) is another VGAM1924 host target gene. SYTL4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SYTL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYTL4 BINDING SITE, designated SEQ ID:28025, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.



[63974] Another function of VGAM1924 is therefore inhibition of Synaptotagmin-like 4 (granuphilin-a) (SYTL4, Accession NM\_080737). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYTL4. TA-KRP (Accession NM\_032505) is another VGAM1924 host target gene. TA-KRP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TA-KRP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TA-KRP BINDING SITE, designated SEQ ID:26253, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63975] Another function of VGAM1924 is therefore inhibition of TA-KRP (Accession NM\_032505). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TA-KRP. TEB4 (Accession XM\_027156) is another VGAM1924 host target gene. TEB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEB4, corresponding to a HOST TARGET bind-

ing site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEB4 BINDING SITE, designated SEQ ID:30427, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63976] Another function of VGAM1924 is therefore inhibition of TEB4 (Accession XM\_027156). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEB4. TGFB-induced Factor 2 (TALE family homeobox) (TGIF2, Accession NM\_021809) is another VGAM1924 host target gene. TGIF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGIF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGIF2 BINDING SITE, designated SEQ ID:22366, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63977] Another function of VGAM1924 is therefore inhibition of TGFB-induced Factor 2 (TALE family homeobox) (TGIF2, Accession NM\_021809). Accordingly, utilities of

VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGIF2. T-cell Lymphoma Invasion and Metastasis 2 (TIAM2, Accession NM\_012454) is another VGAM1924 host target gene. TIAM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIAM2 BINDING SITE, designated SEQ ID:14825, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63978] Another function of VGAM1924 is therefore inhibition of T-cell Lymphoma Invasion and Metastasis 2 (TIAM2, Accession NM\_012454). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIAM2. Toll-like Receptor 10 (TLR10, Accession NM\_030956) is another VGAM1924 host target gene. TLR10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TLR10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLR10 BINDING SITE, designated SEQ ID:25230, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63979] Another function of VGAM1924 is therefore inhibition of Toll-like Receptor 10 (TLR10, Accession NM\_030956). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLR10. Tankyrase, TRF1-interacting Ankyrin-related ADP-ribose Polymerase 2 (TNKS2, Accession NM\_025235) is another VGAM1924 host target gene. TNKS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNKS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNKS2 BINDING SITE, designated SEQ ID:24912, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63980] Another function of VGAM1924 is therefore inhibition of Tankyrase, TRF1-interacting Ankyrin-related ADP-ribose

Polymerase 2 (TNKS2, Accession NM\_025235). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNKS2. TOPBP1 (Accession NM\_007027) is another VGAM1924 host target gene. TOPBP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TOPBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOPBP1 BINDING SITE, designated SEQ ID:13887, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63981] Another function of VGAM1924 is therefore inhibition of TOPBP1 (Accession NM\_007027). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOPBP1. TRAD (Accession NM\_007064) is another VGAM1924 host target gene. TRAD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of TRAD BINDING SITE, designated SEQ ID:13930, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63982] Another function of VGAM1924 is therefore inhibition of TRAD (Accession NM\_007064). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAD. Tripartite Motif-containing 4 (TRIM4, Accession NM\_033017) is another VGAM1924 host target gene. TRIM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM4 BINDING SITE, designated SEQ ID:26902, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63983] Another function of VGAM1924 is therefore inhibition of Tripartite Motif-containing 4 (TRIM4, Accession NM\_033017). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with TRIM4. VDU1 (Accession NM\_015017) is another VGAM1924 host target gene. VDU1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VDU1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VDU1 BINDING SITE, designated SEQ ID:17383, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63984] Another function of VGAM1924 is therefore inhibition of VDU1 (Accession NM\_015017). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VDU1. VEZATIN (Accession NM\_017599) is another VGAM1924 host target gene. VEZATIN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VEZATIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VEZATIN BINDING SITE, designated SEQ ID:19069, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4635.

[63985] Another function of VGAM1924 is therefore inhibition of VEZATIN (Accession NM\_017599). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VEZATIN. Vacuolar Protein Sorting 4B (yeast) (VPS4B, Accession NM\_004869) is another VGAM1924 host target gene. VPS4B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VPS4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VPS4B BINDING SITE, designated SEQ ID:11296, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63986] Another function of VGAM1924 is therefore inhibition of Vacuolar Protein Sorting 4B (yeast) (VPS4B, Accession NM\_004869). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VPS4B. Yes-associated Protein 1, 65kDa (YAP1, Accession NM\_006106) is another VGAM1924 host target gene. YAP1 BINDING SITE is HOST



TARGET binding site found in the 3` untranslated region of mRNA encoded by YAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YAP1 BINDING SITE, designated SEQ ID:12748, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63987] Another function of VGAM1924 is therefore inhibition of Yes-associated Protein 1, 65kDa (YAP1, Accession NM\_006106). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YAP1. Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM\_016353) is another VGAM1924 host target gene. ZDHHC2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZDHHC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC2 BINDING SITE, designated SEQ ID:18493, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63988] Another function of VGAM1924 is therefore inhibition of Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM\_016353). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC2. LOC113763 (Accession NM\_138434) is another VGAM1924 host target gene. LOC113763 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC113763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113763 BINDING SITE, designated SEQ ID:28803, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63989] Another function of VGAM1924 is therefore inhibition of LOC113763 (Accession NM\_138434). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113763. LOC115123 (Accession XM\_055276) is another VGAM1924 host target gene. LOC115123 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC115123, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115123 BINDING SITE, designated SEQ ID:36246, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63990] Another function of VGAM1924 is therefore inhibition of LOC115123 (Accession XM\_055276). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115123. LOC116437 (Accession XM\_058185) is another VGAM1924 host target gene. LOC116437 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116437 BINDING SITE, designated SEQ ID:36580, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63991] Another function of VGAM1924 is therefore inhibition of LOC116437 (Accession XM\_058185). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC116437. LOC119392 (Accession NM\_145247) is another VGAM1924 host target gene. LOC119392 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC119392, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC119392 BINDING SITE, designated SEQ ID:29759, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63992] Another function of VGAM1924 is therefore inhibition of LOC119392 (Accession NM\_145247). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC119392. LOC123283 (Accession XM\_071829) is another VGAM1924 host target gene. LOC123283 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC123283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123283 BINDING SITE, designated SEQ ID:37425, to

the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63993] Another function of VGAM1924 is therefore inhibition of LOC123283 (Accession XM\_071829). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123283. LOC125144 (Accession XM\_058900) is another VGAM1924 host target gene. LOC125144 BINDING SITE1 and LOC125144 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC125144, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC125144 BINDING SITE1 and LOC125144 BINDING SITE2, designated SEQ ID:36788 and SEQ ID:36789 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63994] Another function of VGAM1924 is therefore inhibition of LOC125144 (Accession XM\_058900). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC125144. LOC130589 (Accession NM\_138801) is an-

other VGAM1924 host target gene. LOC130589 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130589, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130589 BINDING SITE, designated SEQ ID:29024, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63995] Another function of VGAM1924 is therefore inhibition of LOC130589 (Accession NM\_138801). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130589. LOC131873 (Accession XM\_067585) is another VGAM1924 host target gene. LOC131873 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC131873, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131873 BINDING SITE, designated SEQ ID:37360, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63996] Another function of VGAM1924 is therefore inhibition of LOC131873 (Accession XM\_067585). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131873. LOC143465 (Accession XM\_096430) is another VGAM1924 host target gene. LOC143465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143465 BINDING SITE, designated SEQ ID:40364, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63997] Another function of VGAM1924 is therefore inhibition of LOC143465 (Accession XM\_096430). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143465. LOC143666 (Accession XM\_096465) is another VGAM1924 host target gene. LOC143666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143666, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143666 BINDING SITE, designated SEQ ID:40369, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63998] Another function of VGAM1924 is therefore inhibition of LOC143666 (Accession XM\_096465). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143666. LOC145134 (Accession XM\_096722) is another VGAM1924 host target gene. LOC145134 BINDING SITE1 and LOC145134 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC145134, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145134 BINDING SITE1 and LOC145134 BINDING SITE2, designated SEQ ID:40500 and SEQ ID:40501 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[63999] Another function of VGAM1924 is therefore inhibition of LOC145134 (Accession XM\_096722). Accordingly, utilities



of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145134. LOC145945 (Accession XM\_096908) is another VGAM1924 host target gene. LOC145945 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145945 BINDING SITE, designated SEQ ID:40637, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64000] Another function of VGAM1924 is therefore inhibition of LOC145945 (Accession XM\_096908). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC146268 (Accession XM\_085397) is another VGAM1924 host target gene. LOC146268 BINDING SITE1 and LOC146268 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC146268, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LOC146268 BINDING SITE1 and LOC146268 BINDING SITE2, designated SEQ ID:38126 and SEQ ID:38123 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64001] Another function of VGAM1924 is therefore inhibition of LOC146268 (Accession XM\_085397). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146268. LOC146952 (Accession XM\_097138) is another VGAM1924 host target gene. LOC146952 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146952, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146952 BINDING SITE, designated SEQ ID:40768, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64002] Another function of VGAM1924 is therefore inhibition of LOC146952 (Accession XM\_097138). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC146952. LOC147219 (Accession XM\_097214) is another VGAM1924 host target gene. LOC147219 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147219 BINDING SITE, designated SEQ ID:40820, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64003] Another function of VGAM1924 is therefore inhibition of LOC147219 (Accession XM\_097214). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147219. LOC147622 (Accession XM\_097255) is another VGAM1924 host target gene. LOC147622 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147622 BINDING SITE, designated SEQ ID:40852, to the nucleotide sequence of VGAM1924 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4635.

[64004] Another function of VGAM1924 is therefore inhibition of LOC147622 (Accession XM\_097255). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147622. LOC147694 (Accession XM\_085843) is another VGAM1924 host target gene. LOC147694 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147694 BINDING SITE, designated SEQ ID:38370, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64005] Another function of VGAM1924 is therefore inhibition of LOC147694 (Accession XM\_085843). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147694. LOC148530 (Accession XM\_097480) is another VGAM1924 host target gene. LOC148530 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148530, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148530 BINDING SITE, designated SEQ ID:40886, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64006] Another function of VGAM1924 is therefore inhibition of LOC148530 (Accession XM\_097480). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148530. LOC149302 (Accession XM\_086489) is another VGAM1924 host target gene. LOC149302 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149302 BINDING SITE, designated SEQ ID:38705, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64007] Another function of VGAM1924 is therefore inhibition of LOC149302 (Accession XM\_086489). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC149302. LOC149332 (Accession XM\_097626) is another VGAM1924 host target gene. LOC149332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149332 BINDING SITE, designated SEQ ID:40983, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64008] Another function of VGAM1924 is therefore inhibition of LOC149332 (Accession XM\_097626). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149332. LOC150170 (Accession XM\_086799) is another VGAM1924 host target gene. LOC150170 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150170 BINDING SITE, designated SEQ ID:38863, to

the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64009] Another function of VGAM1924 is therefore inhibition of LOC150170 (Accession XM\_086799). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150170. LOC150175 (Accession XM\_086806) is another VGAM1924 host target gene. LOC150175 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150175 BINDING SITE, designated SEQ ID:38885, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64010] Another function of VGAM1924 is therefore inhibition of LOC150175 (Accession XM\_086806). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150175. LOC150215 (Accession XM\_086813) is another VGAM1924 host target gene. LOC150215 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC150215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150215 BINDING SITE, designated SEQ ID:38889, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64011] Another function of VGAM1924 is therefore inhibition of LOC150215 (Accession XM\_086813). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150215. LOC150218 (Accession XM\_086850) is another VGAM1924 host target gene. LOC150218 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150218 BINDING SITE, designated SEQ ID:38916, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64012] Another function of VGAM1924 is therefore inhibition of LOC150218 (Accession XM\_086850). Accordingly, utilities



of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150218. LOC150225 (Accession XM\_097870) is another VGAM1924 host target gene. LOC150225 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150225, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150225 BINDING SITE, designated SEQ ID:41191, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64013] Another function of VGAM1924 is therefore inhibition of LOC150225 (Accession XM\_097870). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150225. LOC150311 (Accession XM\_086858) is another VGAM1924 host target gene. LOC150311 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150311, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC150311 BINDING SITE, designated SEQ ID:38926, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64014] Another function of VGAM1924 is therefore inhibition of LOC150311 (Accession XM\_086858). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150311. LOC150397 (Accession XM\_086907) is another VGAM1924 host target gene. LOC150397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150397 BINDING SITE, designated SEQ ID:38963, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64015] Another function of VGAM1924 is therefore inhibition of LOC150397 (Accession XM\_086907). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150397. LOC150418 (Accession XM\_037522) is another VGAM1924 host target gene. LOC150418 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150418 BINDING SITE, designated SEQ ID:32637, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64016] Another function of VGAM1924 is therefore inhibition of LOC150418 (Accession XM\_037522). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150418. LOC150630 (Accession XM\_097931) is another VGAM1924 host target gene. LOC150630 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150630 BINDING SITE, designated SEQ ID:41240, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64017] Another function of VGAM1924 is therefore inhibition of

LOC150630 (Accession XM\_097931). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150630. LOC150819 (Accession XM\_097954) is another VGAM1924 host target gene. LOC150819 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150819, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150819 BINDING SITE, designated SEQ ID:41248, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64018] Another function of VGAM1924 is therefore inhibition of LOC150819 (Accession XM\_097954). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150819. LOC151283 (Accession XM\_087154) is another VGAM1924 host target gene. LOC151283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC151283 BINDING SITE, designated SEQ ID:39092, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64019] Another function of VGAM1924 is therefore inhibition of LOC151283 (Accession XM\_087154). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151283. LOC151429 (Accession XM\_098059) is another VGAM1924 host target gene. LOC151429 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151429 BINDING SITE, designated SEQ ID:41343, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64020] Another function of VGAM1924 is therefore inhibition of LOC151429 (Accession XM\_098059). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151429. LOC152024 (Accession XM\_087365) is an-

other VGAM1924 host target gene. LOC152024 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152024 BINDING SITE, designated SEQ ID:39199, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64021] Another function of VGAM1924 is therefore inhibition of LOC152024 (Accession XM\_087365). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152024. LOC152220 (Accession XM\_098176) is another VGAM1924 host target gene. LOC152220 BINDING SITE1 and LOC152220 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC152220, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152220 BINDING SITE1 and LOC152220 BINDING SITE2, designated SEQ ID:41445 and SEQ ID:41447 respectively, to the nucleotide se-

quence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64022] Another function of VGAM1924 is therefore inhibition of LOC152220 (Accession XM\_098176). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152220. LOC152926 (Accession XM\_087562) is another VGAM1924 host target gene. LOC152926 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152926, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152926 BINDING SITE, designated SEQ ID:39341, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64023] Another function of VGAM1924 is therefore inhibition of LOC152926 (Accession XM\_087562). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152926. LOC154739 (Accession XM\_098602) is another VGAM1924 host target gene. LOC154739 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC154739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154739 BINDING SITE, designated SEQ ID:41723, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64024] Another function of VGAM1924 is therefore inhibition of LOC154739 (Accession XM\_098602). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154739. LOC157858 (Accession XM\_098833) is another VGAM1924 host target gene. LOC157858 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157858 BINDING SITE, designated SEQ ID:41866, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64025] Another function of VGAM1924 is therefore inhibition of LOC157858 (Accession XM\_098833). Accordingly, utilities



of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157858. LOC157918 (Accession XM\_098842) is another VGAM1924 host target gene. LOC157918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157918 BINDING SITE, designated SEQ ID:41897, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64026] Another function of VGAM1924 is therefore inhibition of LOC157918 (Accession XM\_098842). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157918. LOC158014 (Accession XM\_088442) is another VGAM1924 host target gene. LOC158014 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC158014 BINDING SITE, designated SEQ ID:39698, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64027] Another function of VGAM1924 is therefore inhibition of LOC158014 (Accession XM\_088442). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158014. LOC158954 (Accession XM\_017340) is another VGAM1924 host target gene. LOC158954 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158954 BINDING SITE, designated SEQ ID:30314, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64028] Another function of VGAM1924 is therefore inhibition of LOC158954 (Accession XM\_017340). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158954. LOC161003 (Accession NM\_145286) is another VGAM1924 host target gene. LOC161003 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC161003, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161003 BINDING SITE, designated SEQ ID:29803, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64029] Another function of VGAM1924 is therefore inhibition of LOC161003 (Accession NM\_145286). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161003. LOC164971 (Accession XM\_092280) is another VGAM1924 host target gene. LOC164971 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164971 BINDING SITE, designated SEQ ID:40115, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64030] Another function of VGAM1924 is therefore inhibition of

LOC164971 (Accession XM\_092280). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164971. LOC168667 (Accession XM\_166592) is another VGAM1924 host target gene. LOC168667 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC168667, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168667 BINDING SITE, designated SEQ ID:44565, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64031] Another function of VGAM1924 is therefore inhibition of LOC168667 (Accession XM\_166592). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168667. LOC196264 (Accession XM\_113683) is another VGAM1924 host target gene. LOC196264 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196264, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC196264 BINDING SITE, designated SEQ ID:42335, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64032] Another function of VGAM1924 is therefore inhibition of LOC196264 (Accession XM\_113683). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196264. LOC196812 (Accession XM\_116868) is another VGAM1924 host target gene. LOC196812 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196812 BINDING SITE, designated SEQ ID:43138, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64033] Another function of VGAM1924 is therefore inhibition of LOC196812 (Accession XM\_116868). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196812. LOC197319 (Accession XM\_113862) is an-

other VGAM1924 host target gene. LOC197319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197319 BINDING SITE, designated SEQ ID:42476, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64034] Another function of VGAM1924 is therefore inhibition of LOC197319 (Accession XM\_113862). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197319. LOC199678 (Accession XM\_117111) is another VGAM1924 host target gene. LOC199678 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199678 BINDING SITE, designated SEQ ID:43229, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64035] Another function of VGAM1924 is therefore inhibition of LOC199678 (Accession XM\_117111). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199678. LOC200470 (Accession XM\_117235) is another VGAM1924 host target gene. LOC200470 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200470, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200470 BINDING SITE, designated SEQ ID:43311, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64036] Another function of VGAM1924 is therefore inhibition of LOC200470 (Accession XM\_117235). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200470. LOC201895 (Accession XM\_114396) is another VGAM1924 host target gene. LOC201895 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201895, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201895 BINDING SITE, designated SEQ ID:42927, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64037] Another function of VGAM1924 is therefore inhibition of LOC201895 (Accession XM\_114396). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201895. LOC202934 (Accession XM\_117486) is another VGAM1924 host target gene. LOC202934 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202934 BINDING SITE, designated SEQ ID:43468, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64038] Another function of VGAM1924 is therefore inhibition of LOC202934 (Accession XM\_117486). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC202934. LOC203536 (Accession XM\_114716) is another VGAM1924 host target gene. LOC203536 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203536, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203536 BINDING SITE, designated SEQ ID:43058, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64039] Another function of VGAM1924 is therefore inhibition of LOC203536 (Accession XM\_114716). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203536. LOC219790 (Accession XM\_166124) is another VGAM1924 host target gene. LOC219790 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219790, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219790 BINDING SITE, designated SEQ ID:43905, to the nucleotide sequence of VGAM1924 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4635.

[64040] Another function of VGAM1924 is therefore inhibition of LOC219790 (Accession XM\_166124). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219790. LOC221061 (Accession XM\_167709) is another VGAM1924 host target gene. LOC221061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221061 BINDING SITE, designated SEQ ID:44771, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64041] Another function of VGAM1924 is therefore inhibition of LOC221061 (Accession XM\_167709). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221061. LOC221288 (Accession XM\_168058) is another VGAM1924 host target gene. LOC221288 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221288, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221288 BINDING SITE, designated SEQ ID:44968, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64042] Another function of VGAM1924 is therefore inhibition of LOC221288 (Accession XM\_168058). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221288. LOC221474 (Accession XM\_166464) is another VGAM1924 host target gene. LOC221474 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221474, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221474 BINDING SITE, designated SEQ ID:44384, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64043] Another function of VGAM1924 is therefore inhibition of LOC221474 (Accession XM\_166464). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC221474. LOC221830 (Accession XM\_166508) is another VGAM1924 host target gene. LOC221830 BINDING SITE1 and LOC221830 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC221830, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221830 BINDING SITE1 and LOC221830 BINDING SITE2, designated SEQ ID:44436 and SEQ ID:44439 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64044] Another function of VGAM1924 is therefore inhibition of LOC221830 (Accession XM\_166508). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221830. LOC222008 (Accession XM\_168361) is another VGAM1924 host target gene. LOC222008 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222008, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC222008 BINDING SITE, designated SEQ ID:45127, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64045] Another function of VGAM1924 is therefore inhibition of LOC222008 (Accession XM\_168361). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222008. LOC222128 (Accession XM\_166560) is another VGAM1924 host target gene. LOC222128 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222128 BINDING SITE, designated SEQ ID:44542, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64046] Another function of VGAM1924 is therefore inhibition of LOC222128 (Accession XM\_166560). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222128. LOC253019 (Accession XM\_170907) is an-

other VGAM1924 host target gene. LOC253019 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253019 BINDING SITE, designated SEQ ID:45667, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64047] Another function of VGAM1924 is therefore inhibition of LOC253019 (Accession XM\_170907). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253019. LOC253223 (Accession XM\_170515) is another VGAM1924 host target gene. LOC253223 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253223, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253223 BINDING SITE, designated SEQ ID:45346, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64048] Another function of VGAM1924 is therefore inhibition of LOC253223 (Accession XM\_170515). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253223. LOC253258 (Accession XM\_172870) is another VGAM1924 host target gene. LOC253258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253258 BINDING SITE, designated SEQ ID:46147, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64049] Another function of VGAM1924 is therefore inhibition of LOC253258 (Accession XM\_172870). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253258. LOC253260 (Accession XM\_171097) is another VGAM1924 host target gene. LOC253260 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253260, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253260 BINDING SITE, designated SEQ ID:45909, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64050] Another function of VGAM1924 is therefore inhibition of LOC253260 (Accession XM\_171097). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253260. LOC253975 (Accession XM\_171130) is another VGAM1924 host target gene. LOC253975 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253975, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253975 BINDING SITE, designated SEQ ID:45934, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64051] Another function of VGAM1924 is therefore inhibition of LOC253975 (Accession XM\_171130). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC253975. LOC255045 (Accession XM\_171243) is another VGAM1924 host target gene. LOC255045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255045 BINDING SITE, designated SEQ ID:46031, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64052] Another function of VGAM1924 is therefore inhibition of LOC255045 (Accession XM\_171243). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255045. LOC255326 (Accession XM\_172832) is another VGAM1924 host target gene. LOC255326 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255326, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255326 BINDING SITE, designated SEQ ID:46106, to the nucleotide sequence of VGAM1924 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4635.

[64053] Another function of VGAM1924 is therefore inhibition of LOC255326 (Accession XM\_172832). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255326. LOC255465 (Accession XM\_173206) is another VGAM1924 host target gene. LOC255465 BINDING SITE1 and LOC255465 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC255465, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255465 BINDING SITE1 and LOC255465 BINDING SITE2, designated SEQ ID:46460 and SEQ ID:46445 respectively, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64054] Another function of VGAM1924 is therefore inhibition of LOC255465 (Accession XM\_173206). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255465. LOC256273 (Accession XM\_172847) is another VGAM1924 host target gene. LOC256273 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256273 BINDING SITE, designated SEQ ID:46125, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64055] Another function of VGAM1924 is therefore inhibition of LOC256273 (Accession XM\_172847). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256273. LOC256277 (Accession XM\_170644) is another VGAM1924 host target gene. LOC256277 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256277 BINDING SITE, designated SEQ ID:45426, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64056] Another function of VGAM1924 is therefore inhibition of

LOC256277 (Accession XM\_170644). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256277. LOC256733 (Accession XM\_173116) is another VGAM1924 host target gene. LOC256733 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256733, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256733 BINDING SITE, designated SEQ ID:46368, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64057] Another function of VGAM1924 is therefore inhibition of LOC256733 (Accession XM\_173116). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256733. LOC257441 (Accession XM\_170961) is another VGAM1924 host target gene. LOC257441 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC257441 BINDING SITE, designated SEQ ID:45744, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64058] Another function of VGAM1924 is therefore inhibition of LOC257441 (Accession XM\_170961). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257441. LOC257486 (Accession XM\_045029) is another VGAM1924 host target gene. LOC257486 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257486 BINDING SITE, designated SEQ ID:34326, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64059] Another function of VGAM1924 is therefore inhibition of LOC257486 (Accession XM\_045029). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257486. LOC257513 (Accession XM\_175148) is an-

other VGAM1924 host target gene. LOC257513 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257513 BINDING SITE, designated SEQ ID:46640, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64060] Another function of VGAM1924 is therefore inhibition of LOC257513 (Accession XM\_175148). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257513. LOC257567 (Accession XM\_175241) is another VGAM1924 host target gene. LOC257567 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257567, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257567 BINDING SITE, designated SEQ ID:46699, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64061] Another function of VGAM1924 is therefore inhibition of LOC257567 (Accession XM\_175241). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257567. LOC51580 (Accession NM\_015874) is another VGAM1924 host target gene. LOC51580 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51580 BINDING SITE, designated SEQ ID:18014, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64062] Another function of VGAM1924 is therefore inhibition of LOC51580 (Accession NM\_015874). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51580. LOC51634 (Accession NM\_016024) is another VGAM1924 host target gene. LOC51634 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51634, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51634 BINDING SITE, designated SEQ ID:18103, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64063] Another function of VGAM1924 is therefore inhibition of LOC51634 (Accession NM\_016024). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51634. LOC54499 (Accession XM\_047479) is another VGAM1924 host target gene. LOC54499 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC54499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC54499 BINDING SITE, designated SEQ ID:34967, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64064] Another function of VGAM1924 is therefore inhibition of LOC54499 (Accession XM\_047479). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC54499. LOC55885 (Accession NM\_018640) is another VGAM1924 host target gene. LOC55885 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC55885, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC55885 BINDING SITE, designated SEQ ID:20713, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64065] Another function of VGAM1924 is therefore inhibition of LOC55885 (Accession NM\_018640). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC55885. LOC56267 (Accession NM\_019610) is another VGAM1924 host target gene. LOC56267 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC56267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56267 BINDING SITE, designated SEQ ID:21227, to the nucleotide sequence of VGAM1924 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4635.

[64066] Another function of VGAM1924 is therefore inhibition of LOC56267 (Accession NM\_019610). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56267. LOC89932 (Accession XM\_027341) is another VGAM1924 host target gene. LOC89932 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89932 BINDING SITE, designated SEQ ID:30489, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64067] Another function of VGAM1924 is therefore inhibition of LOC89932 (Accession XM\_027341). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89932. LOC90333 (Accession XM\_030958) is another VGAM1924 host target gene. LOC90333 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90333, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90333 BINDING SITE, designated SEQ ID:31223, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64068] Another function of VGAM1924 is therefore inhibition of LOC90333 (Accession XM\_030958). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90333. LOC91149 (Accession XM\_036480) is another VGAM1924 host target gene. LOC91149 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91149, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91149 BINDING SITE, designated SEQ ID:32458, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64069] Another function of VGAM1924 is therefore inhibition of LOC91149 (Accession XM\_036480). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC91149. LOC91286 (Accession XM\_037444) is another VGAM1924 host target gene. LOC91286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91286 BINDING SITE, designated SEQ ID:32624, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64070] Another function of VGAM1924 is therefore inhibition of LOC91286 (Accession XM\_037444). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91286. LOC91496 (Accession XM\_038788) is another VGAM1924 host target gene. LOC91496 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91496, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91496 BINDING SITE, designated SEQ ID:32915, to the

nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64071] Another function of VGAM1924 is therefore inhibition of LOC91496 (Accession XM\_038788). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91496. LOC91549 (Accession XM\_039115) is another VGAM1924 host target gene. LOC91549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91549 BINDING SITE, designated SEQ ID:33012, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64072] Another function of VGAM1924 is therefore inhibition of LOC91549 (Accession XM\_039115). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91549. LOC92231 (Accession XM\_043734) is another VGAM1924 host target gene. LOC92231 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC92231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92231 BINDING SITE, designated SEQ ID:34009, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64073] Another function of VGAM1924 is therefore inhibition of LOC92231 (Accession XM\_043734). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92231. LOC92609 (Accession XM\_053074) is another VGAM1924 host target gene. LOC92609 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92609 BINDING SITE, designated SEQ ID:36061, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64074] Another function of VGAM1924 is therefore inhibition of LOC92609 (Accession XM\_053074). Accordingly, utilities

of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92609. LOC92973 (Accession XM\_048529) is another VGAM1924 host target gene. LOC92973 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC92973, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92973 BINDING SITE, designated SEQ ID:35189, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64075] Another function of VGAM1924 is therefore inhibition of LOC92973 (Accession XM\_048529). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92973. LOC93356 (Accession XM\_050744) is another VGAM1924 host target gene. LOC93356 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC93356, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC93356 BINDING SITE, designated SEQ ID:35672, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64076] Another function of VGAM1924 is therefore inhibition of LOC93356 (Accession XM\_050744). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93356. LOC93380 (Accession XM\_051020) is another VGAM1924 host target gene. LOC93380 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93380, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93380 BINDING SITE, designated SEQ ID:35725, to the nucleotide sequence of VGAM1924 RNA, herein designated VGAM RNA, also designated SEQ ID:4635.

[64077] Another function of VGAM1924 is therefore inhibition of LOC93380 (Accession XM\_051020). Accordingly, utilities of VGAM1924 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93380. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the



present invention, referred to here as Viral Genomic Address Messenger 1925 (VGAM1925) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[64078] VGAM1925 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1925 was detected is described hereinabove with reference to Figs. 1–8.

[64079] VGAM1925 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine Distemper Virus. VGAM1925 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[64080] VGAM1925 gene encodes a VGAM1925 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1925 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1925 precursor RNA is designated SEQ ID:1911, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1911 is located at position 5609 relative to the

genome of Canine Distemper Virus.

[64081] VGAM1925 precursor RNA folds onto itself, forming VGAM1925 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[64082] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1925 folded precursor RNA into VGAM1925 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1925 RNA is designated SEQ ID:4636, and is provided hereinbelow with reference to the sequence listing part.

[64083] VGAM1925 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1925 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1925 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[64084] VGAM1925 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1925 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1925 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1925 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1925 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[64085] The complementary binding of VGAM1925 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1925 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1925 host target RNA into VGAM1925 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[64086] It is appreciated that VGAM1925 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1925 host target genes. The mRNA of each one of this plurality of VGAM1925 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1925 RNA, herein designated VGAM RNA, and which when bound by VGAM1925 RNA causes inhibition of translation of respective one or more VGAM1925 host target proteins.

[64087] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1925 gene, herein designated VGAM GENE, on one or more VGAM1925 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[64088] It is yet further appreciated that a function of VGAM1925 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of viral infection by Canine Distemper Virus. Specific functions, and accordingly utilities, of VGAM1925

correlate with, and may be deduced from, the identity of the host target genes which VGAM1925 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[64089] Nucleotide sequences of the VGAM1925 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1925 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1925 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1925 are further described hereinbelow with reference to Table 1.

[64090] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1925 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1925 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[64091] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1925 gene, herein designated VGAM is inhibition of expression of VGAM1925 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1925 correlate with, and may be deduced

from, the identity of the target genes which VGAM1925 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[64092] A Disintegrin and Metalloproteinase Domain 8 (ADAM8, Accession NM\_001109) is a VGAM1925 host target gene. ADAM8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ADAM8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM8 BINDING SITE, designated SEQ ID:6765, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64093] A function of VGAM1925 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 8 (ADAM8, Accession NM\_001109). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM8. Adenomatosis Polyposis Coli (APC, Accession NM\_000038) is another VGAM1925 host target gene. APC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by APC, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APC BINDING SITE, designated SEQ ID:5483, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64094] Another function of VGAM1925 is therefore inhibition of Adenomatosis Polyposis Coli (APC, Accession NM\_000038). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APC. ADP-ribosylation Factor 3 (ARF3, Accession NM\_001659) is another VGAM1925 host target gene. ARF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARF3 BINDING SITE, designated SEQ ID:7382, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64095] Another function of VGAM1925 is therefore inhibition of ADP-ribosylation Factor 3 (ARF3, Accession NM\_001659).



Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARF3. ATPase, Cu<sup>++</sup> Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM\_000052) is another VGAM1925 host target gene. ATP7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP7A BINDING SITE, designated SEQ ID:5498, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64096] Another function of VGAM1925 is therefore inhibition of ATPase, Cu<sup>++</sup> Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM\_000052). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP7A. Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM\_052988) is another VGAM1925 host target gene. CDK10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDK10, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK10 BINDING SITE, designated SEQ ID:27555, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64097] Another function of VGAM1925 is therefore inhibition of Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM\_052988), a gene which plays a pivotal role in the regulation of the eukaryotic cell cycle. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK10. The function of CDK10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM193. Chromogranin A (parathyroid secretory protein 1) (CHGA, Accession NM\_001275) is another VGAM1925 host target gene. CHGA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CHGA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHGA BIND-

ING SITE, designated SEQ ID:6940, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64098] Another function of VGAM1925 is therefore inhibition of Chromogranin A (parathyroid secretory protein 1) (CHGA, Accession NM\_001275), a gene which regulates dense-core secretory granule biogenesis and hormone sequestration. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHGA. The function of CHGA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM440. Cysteine Knot Superfamily 1, BMP Antagonist 1 (CKTSF1B1, Accession NM\_013372) is another VGAM1925 host target gene. CKTSF1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKTSF1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKTSF1B1 BINDING SITE, designated SEQ ID:15027, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ

ID:4636.

[64099] Another function of VGAM1925 is therefore inhibition of Cysteine Knot Superfamily 1, BMP Antagonist 1 (CKTSF1B1, Accession NM\_013372), a gene which blocks signaling of bone morphogenetic protein (BMP) . Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKTSF1B1. The function of CKTSF1B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28.DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM\_006892) is another VGAM1925 host target gene. DNMT3B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DNMT3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT3B BINDING SITE, designated SEQ ID:13765, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64100] Another function of VGAM1925 is therefore inhibition of

DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM\_006892), a gene which is required for genome wide de novo methylation. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT3B. The function of DNMT3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM280. EGF-like-domain, Multiple 4 (EGFL4, Accession XM\_029883) is another VGAM1925 host target gene. EGFL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL4 BINDING SITE, designated SEQ ID:30969, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64101] Another function of VGAM1925 is therefore inhibition of EGF-like-domain, Multiple 4 (EGFL4, Accession XM\_029883). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with EGFL4. Eukaryotic Translation Initiation Factor 4 Gamma, 2 (EIF4G2, Accession NM\_001418) is another VGAM1925 host target gene. EIF4G2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF4G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4G2 BINDING SITE, designated SEQ ID:7117, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64102] Another function of VGAM1925 is therefore inhibition of Eukaryotic Translation Initiation Factor 4 Gamma, 2 (EIF4G2, Accession NM\_001418), a gene which is a repressor of translation. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF4G2. The function of EIF4G2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1065.Homeo Box D3 (HOXD3, Accession NM\_006898) is another VGAM1925 host target gene.

HOXD3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HOXD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXD3 BINDING SITE, designated SEQ ID:13774, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64103] Another function of VGAM1925 is therefore inhibition of Homeo Box D3 (HOXD3, Accession NM\_006898), a gene which plays a role in the differentiation process of hematopoietic cells. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXD3. The function of HOXD3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1384. Hippocalcin (HPCA, Accession NM\_002143) is another VGAM1925 host target gene. HPCA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HPCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPCA BINDING SITE, designated SEQ ID:7920, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64104] Another function of VGAM1925 is therefore inhibition of Hippocalcin (HPCA, Accession NM\_002143), a gene which may be an hippocampal calcium-binding protein. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPCA. The function of HPCA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM114. Interleukin 13 Receptor, Alpha 1 (IL13RA1, Accession NM\_001560) is another VGAM1925 host target gene. IL13RA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL13RA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL13RA1 BINDING SITE, designated SEQ ID:7286, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also des-



ignated SEQ ID:4636.

[64105] Another function of VGAM1925 is therefore inhibition of Interleukin 13 Receptor, Alpha 1 (IL13RA1, Accession NM\_001560), a gene which binds il-13 with a low affinity. together with il-4r- alpha can form a functional receptor for il-13. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL13RA1. The function of IL13RA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. Interleukin-1 Receptor-associated Kinase 1 (IRAK1, Accession NM\_001569) is another VGAM1925 host target gene. IRAK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRAK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRAK1 BINDING SITE, designated SEQ ID:7301, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64106] Another function of VGAM1925 is therefore inhibition of

Interleukin-1 Receptor-associated Kinase 1 (IRAK1, Accession NM\_001569). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRAK1. Pyrroline-5-carboxylate Reductase 1 (PYCR1, Accession XM\_046472) is another VGAM1925 host target gene. PYCR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PYCR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYCR1 BINDING SITE, designated SEQ ID:34732, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64107] Another function of VGAM1925 is therefore inhibition of Pyrroline-5-carboxylate Reductase 1 (PYCR1, Accession XM\_046472), a gene which catalyzes the NAD(P)H-dependent conversion of pyrroline-5-carboxylate to proline. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYCR1. The function of PYCR1 and its association with various

diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178.RAB36, Member RAS Oncogene Family (RAB36, Accession NM\_004914) is another VGAM1925 host target gene. RAB36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB36 BINDING SITE, designated SEQ ID:11350, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64108] Another function of VGAM1925 is therefore inhibition of RAB36, Member RAS Oncogene Family (RAB36, Accession NM\_004914), a gene which is involved in protein transport. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB36. The function of RAB36 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM129.Transcription Factor AP-2 Gamma (activating

enhancer binding protein 2 gamma) (TFAP2C, Accession NM\_003222) is another VGAM1925 host target gene. TFAP2C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFAP2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFAP2C BINDING SITE, designated SEQ ID:9223, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64109] Another function of VGAM1925 is therefore inhibition of Transcription Factor AP-2 Gamma (activating enhancer binding protein 2 gamma) (TFAP2C, Accession NM\_003222), a gene which is a sequence-specific dna-binding protein that interacts with inducible viral and cellular enhancer elements to regulate transcription of selected genes. Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFAP2C. The function of TFAP2C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM379.Tumor Necrosis Factor (ligand) Superfamily, Member 6 (TNFSF6, Accession NM\_000639) is another VGAM1925 host target gene. TNFSF6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TNFSF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF6 BINDING SITE, designated SEQ ID:6276, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64110] Another function of VGAM1925 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 6 (TNFSF6, Accession NM\_000639). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFSF6. Werner Syndrome (WRN, Accession NM\_000553) is another VGAM1925 host target gene. WRN BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by WRN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WRN BINDING

SITE, designated SEQ ID:6168, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64111] Another function of VGAM1925 is therefore inhibition of Werner Syndrome (WRN, Accession NM\_000553). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WRN. Zic Family Member 3 Heterotaxy 1 (odd-paired homolog, Drosophila) (ZIC3, Accession NM\_003413) is another VGAM1925 host target gene. ZIC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZIC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZIC3 BINDING SITE, designated SEQ ID:9452, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64112] Another function of VGAM1925 is therefore inhibition of Zic Family Member 3 Heterotaxy 1 (odd-paired homolog, Drosophila) (ZIC3, Accession NM\_003413). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with ZIC3. APCL (Accession NM\_005883) is another VGAM1925 host target gene. APCL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by APCL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APCL BINDING SITE, designated SEQ ID:12504, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64113] Another function of VGAM1925 is therefore inhibition of APCL (Accession NM\_005883). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APCL. Ras Homolog Gene Family, Member U (ARHU, Accession NM\_021205) is another VGAM1925 host target gene. ARHU BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARHU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHU BINDING SITE, designated SEQ ID:22185, to the nucleotide sequence of VGAM1925 RNA, herein

designated VGAM RNA, also designated SEQ ID:4636.

[64114] Another function of VGAM1925 is therefore inhibition of Ras Homolog Gene Family, Member U (ARHU, Accession NM\_021205). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHU. Chromosome 1 Open Reading Frame 34 (C1orf34, Accession XM\_027172) is another VGAM1925 host target gene. C1orf34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf34 BINDING SITE, designated SEQ ID:30437, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64115] Another function of VGAM1925 is therefore inhibition of Chromosome 1 Open Reading Frame 34 (C1orf34, Accession XM\_027172). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf34. Chromosome 20 Open Reading Frame 55 (C20orf55, Accession NM\_031424) is another VGAM1925 host target gene.



C20orf55 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf55, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf55 BINDING SITE, designated SEQ ID:25408, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64116] Another function of VGAM1925 is therefore inhibition of Chromosome 20 Open Reading Frame 55 (C20orf55, Accession NM\_031424). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf55. DKFZP434L1435 (Accession XM\_166401) is another VGAM1925 host target gene. DKFZP434L1435 BINDING SITE1 through DKFZP434L1435 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZP434L1435, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L1435 BINDING SITE1 through DKFZP434L1435

BINDING SITE3, designated SEQ ID:44270, SEQ ID:46666 and SEQ ID:46704 respectively, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64117] Another function of VGAM1925 is therefore inhibition of DKFZP434L1435 (Accession XM\_166401). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L1435. ETAA16 (Accession NM\_019002) is another VGAM1925 host target gene. ETAA16 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ETAA16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ETAA16 BINDING SITE, designated SEQ ID:21074, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64118] Another function of VGAM1925 is therefore inhibition of ETAA16 (Accession NM\_019002). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ETAA16. FASTK (Accession NM\_025096) is another

VGAM1925 host target gene. FASTK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FASTK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FASTK BINDING SITE, designated SEQ ID:24731, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64119] Another function of VGAM1925 is therefore inhibition of FASTK (Accession NM\_025096). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FASTK. FLJ13491 (Accession NM\_024623) is another VGAM1925 host target gene. FLJ13491 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13491, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13491 BINDING SITE, designated SEQ ID:23890, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64120] Another function of VGAM1925 is therefore inhibition of FLJ13491 (Accession NM\_024623). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13491. FLJ14154 (Accession NM\_024845) is another VGAM1925 host target gene. FLJ14154 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14154 BINDING SITE, designated SEQ ID:24273, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64121] Another function of VGAM1925 is therefore inhibition of FLJ14154 (Accession NM\_024845). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14154. FLJ20343 (Accession NM\_017775) is another VGAM1925 host target gene. FLJ20343 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20343, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20343 BINDING SITE, designated SEQ ID:19401, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64122] Another function of VGAM1925 is therefore inhibition of FLJ20343 (Accession NM\_017775). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20343. FLJ22479 (Accession NM\_024900) is another VGAM1925 host target gene. FLJ22479 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22479 BINDING SITE, designated SEQ ID:24388, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64123] Another function of VGAM1925 is therefore inhibition of FLJ22479 (Accession NM\_024900). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ22479. FLJ23091 (Accession NM\_024911) is another VGAM1925 host target gene. FLJ23091 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23091 BINDING SITE, designated SEQ ID:24419, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64124] Another function of VGAM1925 is therefore inhibition of FLJ23091 (Accession NM\_024911). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23091. Guanine Nucleotide Binding Protein (G protein), Gamma 4 (GNG4, Accession NM\_004485) is another VGAM1925 host target gene. GNG4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GNG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNG4 BINDING SITE, designated SEQ ID:10814, to the nucleotide sequence of

VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64125] Another function of VGAM1925 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Gamma 4 (GNG4, Accession NM\_004485). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNG4. HSPF2 (Accession NM\_005528) is another VGAM1925 host target gene. HSPF2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPF2 BINDING SITE, designated SEQ ID:12049, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64126] Another function of VGAM1925 is therefore inhibition of HSPF2 (Accession NM\_005528). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPF2. Interleukin 1 Receptor Accessory Protein-like 1 (IL1RAPL1, Accession NM\_014271) is another VGAM1925 host target

gene. IL1RAPL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IL1RAPL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1RAPL1 BINDING SITE, designated SEQ ID:15556, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64127] Another function of VGAM1925 is therefore inhibition of Interleukin 1 Receptor Accessory Protein-like 1 (IL1RAPL1, Accession NM\_014271). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1RAPL1. KIAA0408 (Accession NM\_014702) is another VGAM1925 host target gene. KIAA0408 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0408 BINDING SITE, designated SEQ ID:16236, to the nucleotide sequence of VGAM1925 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4636.

[64128] Another function of VGAM1925 is therefore inhibition of KIAA0408 (Accession NM\_014702). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0408. KIAA0855 (Accession NM\_015003) is another VGAM1925 host target gene. KIAA0855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0855 BINDING SITE, designated SEQ ID:17378, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64129] Another function of VGAM1925 is therefore inhibition of KIAA0855 (Accession NM\_015003). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0855. KIAA1026 (Accession XM\_048825) is another VGAM1925 host target gene. KIAA1026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1026, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1026 BINDING SITE, designated SEQ ID:35278, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64130] Another function of VGAM1925 is therefore inhibition of KIAA1026 (Accession XM\_048825). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1026. KIAA1203 (Accession XM\_049683) is another VGAM1925 host target gene. KIAA1203 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1203, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1203 BINDING SITE, designated SEQ ID:35474, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64131] Another function of VGAM1925 is therefore inhibition of KIAA1203 (Accession XM\_049683). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1203. KIAA1340 (Accession XM\_044836) is another VGAM1925 host target gene. KIAA1340 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1340 BINDING SITE, designated SEQ ID:34301, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64132] Another function of VGAM1925 is therefore inhibition of KIAA1340 (Accession XM\_044836). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1340. MGC10715 (Accession NM\_024325) is another VGAM1925 host target gene. MGC10715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10715 BINDING SITE, designated SEQ ID:23617, to

the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64133] Another function of VGAM1925 is therefore inhibition of MGC10715 (Accession NM\_024325). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10715. MGC2603 (Accession NM\_024037) is another VGAM1925 host target gene. MGC2603 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2603, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2603 BINDING SITE, designated SEQ ID:23472, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64134] Another function of VGAM1925 is therefore inhibition of MGC2603 (Accession NM\_024037). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2603. N4BP3 (Accession XM\_038920) is another VGAM1925 host target gene. N4BP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by N4BP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP3 BINDING SITE, designated SEQ ID:32941, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64135] Another function of VGAM1925 is therefore inhibition of N4BP3 (Accession XM\_038920). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP3. PANK (Accession NM\_138316) is another VGAM1925 host target gene. PANK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PANK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PANK BINDING SITE, designated SEQ ID:28716, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64136] Another function of VGAM1925 is therefore inhibition of PANK (Accession NM\_138316). Accordingly, utilities of

VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PANK. Protein Tyrosine Phosphatase, Receptor Type, F Polypeptide (PTPRF), Interacting Protein (liprin), Alpha 4 (PPFIA4, Accession XM\_046751) is another VGAM1925 host target gene. PPFIA4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPFIA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPFIA4 BINDING SITE, designated SEQ ID:34824, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64137] Another function of VGAM1925 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, F Polypeptide (PTPRF), Interacting Protein (liprin), Alpha 4 (PPFIA4, Accession XM\_046751). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPFIA4. RHO6 (Accession NM\_014470) is another VGAM1925 host target gene. RHO6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded

by RHO6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHO6 BINDING SITE, designated SEQ ID:15821, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64138] Another function of VGAM1925 is therefore inhibition of RHO6 (Accession NM\_014470). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHO6. Ring Finger Protein 24 (RNF24, Accession NM\_007219) is another VGAM1925 host target gene. RNF24 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RNF24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF24 BINDING SITE, designated SEQ ID:14087, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64139] Another function of VGAM1925 is therefore inhibition of Ring Finger Protein 24 (RNF24, Accession NM\_007219).

Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF24. RoXaN (Accession NM\_025013) is another VGAM1925 host target gene. RoXaN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RoXaN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RoXaN BINDING SITE, designated SEQ ID:24605, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64140] Another function of VGAM1925 is therefore inhibition of RoXaN (Accession NM\_025013). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RoXaN. Signal Transducer and Activator of Transcription 5A (STAT5A, Accession NM\_003152) is another VGAM1925 host target gene. STAT5A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAT5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or



BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAT5A BINDING SITE, designated SEQ ID:9129, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64141] Another function of VGAM1925 is therefore inhibition of Signal Transducer and Activator of Transcription 5A (STAT5A, Accession NM\_003152). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAT5A. Synaptotagmin-like 2 (SYTL2, Accession NM\_032379) is another VGAM1925 host target gene. SYTL2 BINDING SITE1 and SYTL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SYTL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYTL2 BINDING SITE1 and SYTL2 BINDING SITE2, designated SEQ ID:26175 and SEQ ID:26759 respectively, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64142] Another function of VGAM1925 is therefore inhibition of

Synaptotagmin-like 2 (SYTL2, Accession NM\_032379). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYTL2. Tubulin, Gamma Complex Associated Protein 3 (TUBGCP3, Accession NM\_006322) is another VGAM1925 host target gene. TUBGCP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUBGCP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUBGCP3 BINDING SITE, designated SEQ ID:13014, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64143] Another function of VGAM1925 is therefore inhibition of Tubulin, Gamma Complex Associated Protein 3 (TUBGCP3, Accession NM\_006322). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUBGCP3. UPLC1 (Accession NM\_017707) is another VGAM1925 host target gene. UPLC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UPLC1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UPLC1 BINDING SITE, designated SEQ ID:19285, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64144] Another function of VGAM1925 is therefore inhibition of UPLC1 (Accession NM\_017707). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UPLC1. LOC121344 (Accession XM\_058555) is another VGAM1925 host target gene. LOC121344 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC121344, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121344 BINDING SITE, designated SEQ ID:36658, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64145] Another function of VGAM1925 is therefore inhibition of LOC121344 (Accession XM\_058555). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC121344. LOC124976 (Accession XM\_058879) is another VGAM1925 host target gene. LOC124976 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124976 BINDING SITE, designated SEQ ID:36785, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64146] Another function of VGAM1925 is therefore inhibition of LOC124976 (Accession XM\_058879). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124976. LOC127845 (Accession XM\_059186) is another VGAM1925 host target gene. LOC127845 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC127845, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127845 BINDING SITE, designated SEQ ID:36912, to

the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64147] Another function of VGAM1925 is therefore inhibition of LOC127845 (Accession XM\_059186). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127845. LOC137964 (Accession XM\_059933) is another VGAM1925 host target gene. LOC137964 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC137964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC137964 BINDING SITE, designated SEQ ID:37113, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64148] Another function of VGAM1925 is therefore inhibition of LOC137964 (Accession XM\_059933). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC137964. LOC139231 (Accession XM\_060020) is another VGAM1925 host target gene. LOC139231 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC139231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139231 BINDING SITE, designated SEQ ID:37143, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64149] Another function of VGAM1925 is therefore inhibition of LOC139231 (Accession XM\_060020). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139231. LOC144266 (Accession XM\_084795) is another VGAM1925 host target gene. LOC144266 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144266 BINDING SITE, designated SEQ ID:37712, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64150] Another function of VGAM1925 is therefore inhibition of LOC144266 (Accession XM\_084795). Accordingly, utilities

of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144266. LOC145826 (Accession XM\_096875) is another VGAM1925 host target gene. LOC145826 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145826 BINDING SITE, designated SEQ ID:40610, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64151] Another function of VGAM1925 is therefore inhibition of LOC145826 (Accession XM\_096875). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145826. LOC148113 (Accession XM\_086058) is another VGAM1925 host target gene. LOC148113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC148113 BINDING SITE, designated SEQ ID:38472, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64152] Another function of VGAM1925 is therefore inhibition of LOC148113 (Accession XM\_086058). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148113. LOC149566 (Accession XM\_097670) is another VGAM1925 host target gene. LOC149566 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149566 BINDING SITE, designated SEQ ID:41019, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64153] Another function of VGAM1925 is therefore inhibition of LOC149566 (Accession XM\_097670). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149566. LOC152633 (Accession XM\_098248) is another VGAM1925 host target gene. LOC152633 BINDING



SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152633, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152633 BINDING SITE, designated SEQ ID:41535, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64154] Another function of VGAM1925 is therefore inhibition of LOC152633 (Accession XM\_098248). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152633. LOC153711 (Accession XM\_098419) is another VGAM1925 host target gene. LOC153711 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153711 BINDING SITE, designated SEQ ID:41670, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64155] Another function of VGAM1925 is therefore inhibition of

LOC153711 (Accession XM\_098419). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153711. LOC159148 (Accession XM\_099030) is another VGAM1925 host target gene. LOC159148 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC159148, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159148 BINDING SITE, designated SEQ ID:42079, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64156] Another function of VGAM1925 is therefore inhibition of LOC159148 (Accession XM\_099030). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159148. LOC196283 (Accession XM\_113684) is another VGAM1925 host target gene. LOC196283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC196283 BINDING SITE, designated SEQ ID:42341, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64157] Another function of VGAM1925 is therefore inhibition of LOC196283 (Accession XM\_113684). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196283. LOC197358 (Accession XM\_113872) is another VGAM1925 host target gene. LOC197358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197358 BINDING SITE, designated SEQ ID:42511, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64158] Another function of VGAM1925 is therefore inhibition of LOC197358 (Accession XM\_113872). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197358. LOC201799 (Accession XM\_114380) is an-

other VGAM1925 host target gene. LOC201799 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201799, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201799 BINDING SITE, designated SEQ ID:42918, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64159] Another function of VGAM1925 is therefore inhibition of LOC201799 (Accession XM\_114380). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201799. LOC201965 (Accession XM\_114412) is another VGAM1925 host target gene. LOC201965 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201965, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201965 BINDING SITE, designated SEQ ID:42936, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64160] Another function of VGAM1925 is therefore inhibition of LOC201965 (Accession XM\_114412). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201965. LOC253891 (Accession XM\_170485) is another VGAM1925 host target gene. LOC253891 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253891 BINDING SITE, designated SEQ ID:45324, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64161] Another function of VGAM1925 is therefore inhibition of LOC253891 (Accession XM\_170485). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253891. LOC253897 (Accession XM\_171187) is another VGAM1925 host target gene. LOC253897 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253897, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253897 BINDING SITE, designated SEQ ID:45969, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64162] Another function of VGAM1925 is therefore inhibition of LOC253897 (Accession XM\_171187). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253897. LOC256806 (Accession XM\_172865) is another VGAM1925 host target gene. LOC256806 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256806, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256806 BINDING SITE, designated SEQ ID:46142, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64163] Another function of VGAM1925 is therefore inhibition of LOC256806 (Accession XM\_172865). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC256806. LOC51608 (Accession XM\_033102) is another VGAM1925 host target gene. LOC51608 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51608, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51608 BINDING SITE, designated SEQ ID:31841, to the nucleotide sequence of VGAM1925 RNA, herein designated VGAM RNA, also designated SEQ ID:4636.

[64164] Another function of VGAM1925 is therefore inhibition of LOC51608 (Accession XM\_033102). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51608. LOC91694 (Accession XM\_040082) is another VGAM1925 host target gene. LOC91694 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91694 BINDING SITE, designated SEQ ID:33251, to the nucleotide sequence of VGAM1925 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4636.

[64165] Another function of VGAM1925 is therefore inhibition of LOC91694 (Accession XM\_040082). Accordingly, utilities of VGAM1925 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91694. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1926 (VGAM1926) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[64166] VGAM1926 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1926 was detected is described hereinabove with reference to Figs. 1–8.

[64167] VGAM1926 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine Distemper Virus. VGAM1926 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[64168] VGAM1926 gene encodes a VGAM1926 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other



miRNA genes, and unlike most ordinary genes, VGAM1926 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1926 precursor RNA is designated SEQ ID:1912, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1912 is located at position 8304 relative to the genome of Canine Distemper Virus.

[64169] VGAM1926 precursor RNA folds onto itself, forming VGAM1926 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[64170] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1926 folded precursor RNA into VGAM1926 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1926 RNA is designated SEQ ID:4637, and is provided hereinbelow with reference to the sequence listing part.

[64171] VGAM1926 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1926 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1926 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[64172] VGAM1926 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1926 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1926 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1926 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1926 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[64173] The complementary binding of VGAM1926 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1926 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1926 host target RNA into VGAM1926 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[64174] It is appreciated that VGAM1926 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1926 host target genes. The mRNA of

each one of this plurality of VGAM1926 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1926 RNA, herein designated VGAM RNA, and which when bound by VGAM1926 RNA causes inhibition of translation of respective one or more VGAM1926 host target proteins.

[64175] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1926 gene, herein designated VGAM GENE, on one or more VGAM1926 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[64176] It is yet further appreciated that a function of VGAM1926 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1926 include diagnosis, prevention and treatment of viral infection by Canine Distemper Virus. Specific functions, and accordingly utilities, of VGAM1926 correlate with, and may be deduced from, the identity of the host target genes which VGAM1926 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[64177] Nucleotide sequences of the VGAM1926 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1926 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1926 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1926 are further described hereinbelow with reference to Table 1.

[64178] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1926 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1926 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[64179] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1926 gene, herein designated VGAM is inhibition of expression of VGAM1926 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1926 correlate with, and may be deduced from, the identity of the target genes which VGAM1926 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[64180] Glycoprotein A Repetitions Predominant (GARP, Accession NM\_005512) is a VGAM1926 host target gene. GARP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GARP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GARP BINDING SITE, designated SEQ ID:12035, to the nucleotide sequence of VGAM1926 RNA, herein designated VGAM RNA, also designated SEQ ID:4637.

[64181] A function of VGAM1926 is therefore inhibition of Glycoprotein A Repetitions Predominant (GARP, Accession NM\_005512). Accordingly, utilities of VGAM1926 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with GARP. ARPP-21 (Accession NM\_016300) is another VGAM1926 host target gene.

ARPP-21 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARPP-21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARPP-21 BINDING SITE, designated SEQ ID:18421, to the nucleotide sequence of VGAM1926 RNA, herein designated VGAM RNA, also designated SEQ ID:4637.

[64182] Another function of VGAM1926 is therefore inhibition of ARPP-21 (Accession NM\_016300). Accordingly, utilities of VGAM1926 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARPP-21. KIAA1577 (Accession XM\_035299) is another VGAM1926 host target gene. KIAA1577 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1577 BINDING SITE, designated SEQ ID:32209, to the nucleotide sequence of VGAM1926 RNA, herein designated VGAM RNA, also designated SEQ ID:4637.

[64183] Another function of VGAM1926 is therefore inhibition of KIAA1577 (Accession XM\_035299). Accordingly, utilities of VGAM1926 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1577. MGC4400 (Accession NM\_032679) is another VGAM1926 host target gene. MGC4400 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4400, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4400 BINDING SITE, designated SEQ ID:26399, to the nucleotide sequence of VGAM1926 RNA, herein designated VGAM RNA, also designated SEQ ID:4637.

[64184] Another function of VGAM1926 is therefore inhibition of MGC4400 (Accession NM\_032679). Accordingly, utilities of VGAM1926 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4400. LOC145622 (Accession XM\_085186) is another VGAM1926 host target gene. LOC145622 BINDING SITE1



and LOC145622 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC145622, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145622 BINDING SITE1 and LOC145622 BINDING SITE2, designated SEQ ID:37905 and SEQ ID:37906 respectively, to the nucleotide sequence of VGAM1926 RNA, herein designated VGAM RNA, also designated SEQ ID:4637.

[64185] Another function of VGAM1926 is therefore inhibition of LOC145622 (Accession XM\_085186). Accordingly, utilities of VGAM1926 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145622. WSB1 (Accession NM\_134265) is another VGAM1927 host target gene. WSB1 BINDING SITE1 and WSB1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WSB1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WSB1 BINDING SITE1 and WSB1 BINDING SITE2, designated SEQ ID:28620 and SEQ ID:28614 respectively,

to the nucleotide sequence of VGAM1927 RNA, herein designated VGAM RNA, also designated SEQ ID:4638.

[64186] Another function of VGAM1927 is therefore inhibition of WSB1 (Accession NM\_134265). Accordingly, utilities of VGAM1927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WSB1. LOC144997 (Accession XM\_096702) is another VGAM1927 host target gene. LOC144997 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144997, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144997 BINDING SITE, designated SEQ ID:40482, to the nucleotide sequence of VGAM1927 RNA, herein designated VGAM RNA, also designated SEQ ID:4638.

[64187] Another function of VGAM1927 is therefore inhibition of LOC144997 (Accession XM\_096702). Accordingly, utilities of VGAM1927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144997. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1928 (VGAM1928) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[64188] VGAM1928 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1928 was detected is described hereinabove with reference to Figs. 1–8.

[64189] VGAM1928 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine Distemper Virus. VGAM1928 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[64190] VGAM1928 gene encodes a VGAM1928 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1928 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1928 precursor RNA is designated SEQ ID:1914, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1914 is located at position 5392 relative to the genome of Canine Distemper Virus.

[64191] VGAM1928 precursor RNA folds onto itself, forming VGAM1928 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[64192] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1928 folded precursor RNA into VGAM1928 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1928 RNA is designated SEQ ID:4639, and is provided hereinbelow with reference to the sequence listing part.

[64193] VGAM1928 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1928 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1928 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[64194] VGAM1928 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1928 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1928 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1928 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1928 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[64195] The complementary binding of VGAM1928 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1928 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1928 host target RNA into VGAM1928 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[64196] It is appreciated that VGAM1928 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1928 host target genes. The mRNA of each one of this plurality of VGAM1928 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1928 RNA, herein designated VGAM RNA, and which when bound by VGAM1928 RNA causes inhibition of translation of respective one or more VGAM1928 host target proteins.

[64197] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1928 gene, herein designated VGAM GENE, on one or more VGAM1928 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[64198] It is yet further appreciated that a function of VGAM1928 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of viral infection by Canine Distemper Virus. Specific functions, and accordingly utilities, of VGAM1928 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1928 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[64199] Nucleotide sequences of the VGAM1928 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1928 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1928 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1928 are further described hereinbelow with reference to Table 1.

[64200] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1928 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1928 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[64201] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1928 gene, herein designated VGAM is inhibition of expression of VGAM1928 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1928 correlate with, and may be deduced from, the identity of the target genes which VGAM1928



binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[64202] Adenosine Deaminase, RNA-specific (ADAR, Accession NM\_001111) is a VGAM1928 host target gene. ADAR BINDING SITE1 through ADAR BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADAR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAR BINDING SITE1 through ADAR BINDING SITE3, designated SEQ ID:6772, SEQ ID:17958 and SEQ ID:17965 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64203] A function of VGAM1928 is therefore inhibition of Adenosine Deaminase, RNA-specific (ADAR, Accession NM\_001111), a gene which converts adenosine to inosine in double-stranded RNA. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAR. The function of ADAR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM323.A Kinase (PRKA) Anchor Protein 2 (AKAP2, Accession NM\_007203) is another VGAM1928 host target gene. AKAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP2 BINDING SITE, designated SEQ ID:14061, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64204] Another function of VGAM1928 is therefore inhibition of A Kinase (PRKA) Anchor Protein 2 (AKAP2, Accession NM\_007203), a gene which binds to regulatory subunit (rii) of protein kinase a. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP2. The function of AKAP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18.Aldehyde Dehydrogenase 3 Family, Member B2 (ALDH3B2, Accession NM\_000695) is another VGAM1928 host target gene. ALDH3B2 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ALDH3B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH3B2 BINDING SITE, designated SEQ ID:6357, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64205] Another function of VGAM1928 is therefore inhibition of Aldehyde Dehydrogenase 3 Family, Member B2 (ALDH3B2, Accession NM\_000695), a gene which may play a role in alcohol detoxitation. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH3B2. The function of ALDH3B2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM251. Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM\_001282) is another VGAM1928 host target gene. AP2B1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AP2B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP2B1 BINDING SITE, designated SEQ ID:6954, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64206] Another function of VGAM1928 is therefore inhibition of Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM\_001282), a gene which links clathrin to receptors in coated vesicles. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP2B1. The function of AP2B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1126. Aprataxin (APTX, Accession NM\_017692) is another VGAM1928 host target gene. APTX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APTX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APTX BINDING SITE, designated SEQ ID:19248, to the nucleotide sequence of VGAM1928 RNA, herein

designated VGAM RNA, also designated SEQ ID:4639.

[64207] Another function of VGAM1928 is therefore inhibition of Aprataxin (APTX, Accession NM\_017692). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APTX. Apical Protein-like (Xenopus laevis) (APXL, Accession NM\_001649) is another VGAM1928 host target gene. APXL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APXL BINDING SITE, designated SEQ ID:7357, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64208] Another function of VGAM1928 is therefore inhibition of Apical Protein-like (Xenopus laevis) (APXL, Accession NM\_001649), a gene which is implicated in amiloride-sensitive sodium channel activity. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APXL. The function of APXL and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM152. Beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_018644) is another VGAM1928 host target gene. B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GAT1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2, designated SEQ ID:20719 and SEQ ID:27631 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64209] Another function of VGAM1928 is therefore inhibition of Beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_018644). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GAT1. Brain and Acute Leukemia, Cytoplasmic (BAALC, Accession NM\_024812) is another VGAM1928 host target gene. BAALC BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by BAALC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAALC BINDING SITE, designated SEQ ID:24196, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64210] Another function of VGAM1928 is therefore inhibition of Brain and Acute Leukemia, Cytoplasmic (BAALC, Accession NM\_024812). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAALC. B-cell CLL/lymphoma 2 (BCL2, Accession NM\_000633) is another VGAM1928 host target gene. BCL2 BINDING SITE1 and BCL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BCL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2 BINDING SITE1 and BCL2 BINDING SITE2, designated SEQ ID:6251 and SEQ ID:6258 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64211] Another function of VGAM1928 is therefore inhibition of B-cell CLL/lymphoma 2 (BCL2, Accession NM\_000633). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2. Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM\_005093) is another VGAM1928 host target gene. CBFA2T2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFA2T2 BINDING SITE, designated SEQ ID:11549, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64212] Another function of VGAM1928 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM\_005093), a gene which is a putative transcription factor. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T2. The function of CBFA2T2 and its associa-



tion with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM152.CD28 Antigen (Tp44) (CD28, Accession NM\_006139) is another VGAM1928 host target gene. CD28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD28 BINDING SITE, designated SEQ ID:12784, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64213] Another function of VGAM1928 is therefore inhibition of CD28 Antigen (Tp44) (CD28, Accession NM\_006139), a gene which possibly involved in t-cell activation. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD28. The function of CD28 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM281. CD44 Antigen (homing function and Indian blood group system) (CD44, Accession NM\_000610) is another VGAM1928 host target gene. CD44 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD44, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD44 BINDING SITE, designated SEQ ID:6211, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64214] Another function of VGAM1928 is therefore inhibition of CD44 Antigen (homing function and Indian blood group system) (CD44, Accession NM\_000610), a gene which is main cell surface receptor for hyaluronate, and involves in

matrix adhesion, lymphocyte activation and lymph node homing. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD44. The function of CD44 has been established by previous studies. Weber et al. (1996) noted that the CD44 gene encodes a transmembrane protein that is expressed as a family of molecular isoforms generated from alternative RNA splicing and posttranslational modifications. Certain CD44 isoforms that regulate activation and migration of lymphocytes and macrophages may also enhance local growth and metastatic spread of tumor cells. One ligand of CD44 is hyaluronic acid, binding of which to the NH<sub>2</sub>-terminal domain of CD44 enhances cellular aggregation and tumor cell growth. (Krainer et al. (1991) referred to CD44 as a 'hyaladherin' -- see 601269.) Weber et al. (1996) demonstrated that another ligand is osteopontin (OMIM Ref. No. 166490). Osteopontin induces cellular chemotaxis but not homotypic aggregation of cells, whereas the inverse is true for the interaction between CD44 and hyaluronate. The alternative responses to CD44 ligation may be exploited by tumor cells to allow OPN-mediated metastatic spread and hyaluronate-dependent growth in newly colo-

nized tissues in the process of tumor metastasis Animal model experiments lend further support to the function of CD44. Schmits et al. (1997) generated mice deficient in all known isoforms of Cd44 by targeting exons encoding the invariant N-terminal region of the molecule. Mice were born in mendelian ratio without any obvious developmental or neurologic deficits. Hematologic impairment was evidenced by altered tissue distribution of myeloid progenitors with increased levels of colony-forming unit-granulocyte-macrophage in bone marrow and reduced numbers in spleen. Fetal liver colony-forming unit-spleen and granulocyte colony-stimulating factor mobilization assays, together with reduced colony-forming unit-granulocyte-macrophage in peripheral blood, suggested that progenitor egress from the bone marrow was defective. Mice also developed exaggerated granuloma responses to *Cryptosporidium parvum* infection. Tumor studies showed that SV40-transformed Cd44-deficient fibroblasts were highly tumorigenic in nude mice, whereas reintroduction of Cd44 expression into these fibroblasts resulted in a dramatic inhibition of tumor growth.

[64215] It is appreciated that the abovementioned animal model for CD44 is acknowledged by those skilled in the art as a

scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[64216] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64217] Weber, G. F.; Ashkar, S.; Glimcher, M. J.; Cantor, H. : Receptor–ligand interaction between CD44 and osteopontin (Eta-1). Science 271: 509–512, 1996. ; and

[64218] Schmits, R.; Filmus, J.; Gerwin, N.; Senaldi, G.; Kiefer, F.; Kundig, T.; Wakeham, A.; Shahinian, A.; Catzavelos, C.; Rak, J.; Furlonger, C.; Zakarian, A.; Simard, J. J.; Ohashi, P. S.

[64219] Further studies establishing the function and utilities of CD44 are found in John Hopkins OMIM database record ID 107269, and in cited publications numbered 210–215, 5262–223, 4163–416 and 4205 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cyclin–dependent Kinase Inhibitor 2A (melanoma, p16, inhibits CDK4) (CDKN2A, Accession NM\_058195) is another VGAM1928 host target gene. CDKN2A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CDKN2A, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN2A BINDING SITE, designated SEQ ID:27756, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64220] Another function of VGAM1928 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 2A (melanoma, p16, inhibits CDK4) (CDKN2A, Accession NM\_058195). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN2A. Cadherin, EGF LAG Seven-pass G-type Receptor 1 (flamingo homolog, Drosophila) (CELSR1, Accession NM\_014246) is another VGAM1928 host target gene. CELSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CELSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CELSR1 BINDING SITE, designated SEQ ID:15518, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64221] Another function of VGAM1928 is therefore inhibition of Cadherin, EGF LAG Seven-pass G-type Receptor 1 (flamingo homolog, Drosophila) (CELSR1, Accession NM\_014246), a gene which is involved in contact-mediated communication. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CELSR1. The function of CELSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM459. Chimerin (chimaerin) 1 (CHN1, Accession NM\_001822) is another VGAM1928 host target gene. CHN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CHN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHN1 BINDING SITE, designated SEQ ID:7561, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64222] Another function of VGAM1928 is therefore inhibition of Chimerin (chimaerin) 1 (CHN1, Accession NM\_001822), a gene which may play an important role in neuronal signal-

transduction mechanisms. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHN1. The function of CHN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM632. Cytoskeleton-associated Protein 1 (CKAP1, Accession XM\_056494) is another VGAM1928 host target gene. CKAP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CKAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKAP1 BINDING SITE, designated SEQ ID:36400, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64223] Another function of VGAM1928 is therefore inhibition of Cytoskeleton-associated Protein 1 (CKAP1, Accession XM\_056494). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKAP1. Chloride Channel 5 (nephrolithiasis 2, X-linked, Dent disease) (CLCN5, Acces-



sion NM\_000084) is another VGAM1928 host target gene. CLCN5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLCN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN5 BINDING SITE, designated SEQ ID:5536, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64224] Another function of VGAM1928 is therefore inhibition of Chloride Channel 5 (nephrolithiasis 2, X-linked, Dent disease) (CLCN5, Accession NM\_000084), a gene which may interfere in renal tubular function. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCN5. The function of CLCN5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM48. Collagen, Type IV, Alpha 4 (COL4A4, Accession NM\_000092) is another VGAM1928 host target gene. COL4A4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

COL4A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A4 BINDING SITE, designated SEQ ID:5551, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64225] Another function of VGAM1928 is therefore inhibition of Collagen, Type IV, Alpha 4 (COL4A4, Accession NM\_000092). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A4. Collagen, Type IV, Alpha 5 (Alport syndrome) (COL4A5, Accession NM\_000495) is another VGAM1928 host target gene. COL4A5 BINDING SITE1 through COL4A5 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL4A5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A5 BINDING SITE1 through COL4A5 BINDING SITE3, designated SEQ ID:6109, SEQ ID:27215 and SEQ ID:27212 respectively, to the nucleotide sequence of VGAM1928 RNA,

herein designated VGAM RNA, also designated SEQ ID:4639.

[64226] Another function of VGAM1928 is therefore inhibition of Collagen, Type IV, Alpha 5 (Alport syndrome) (COL4A5, Accession NM\_000495). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A5. Cytochrome P450, 51 (lanosterol 14-alpha-demethylase) (CYP51, Accession NM\_000786) is another VGAM1928 host target gene. CYP51 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CYP51, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP51 BINDING SITE, designated SEQ ID:6437, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64227] Another function of VGAM1928 is therefore inhibition of Cytochrome P450, 51 (lanosterol 14-alpha-demethylase) (CYP51, Accession NM\_000786). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP51.

Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM\_166434) is another VGAM1928 host target gene. DAAM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAAM2 BINDING SITE, designated SEQ ID:44332, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64228] Another function of VGAM1928 is therefore inhibition of Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM\_166434), a gene which controls cell polarity and movement during development. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAAM2. The function of DAAM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Diacylglycerol Kinase, Gamma 90kDa (DGKG, Accession NM\_001346) is another VGAM1928 host target gene. DGKG BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by DGKG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKG BINDING SITE, designated SEQ ID:7028, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64229] Another function of VGAM1928 is therefore inhibition of Diacylglycerol Kinase, Gamma 90kDa (DGKG, Accession NM\_001346), a gene which may convert diacylglycerol to phosphatidic acid. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKG. The function of DGKG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM451. Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM\_004423) is another VGAM1928 host target gene. DVL3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DVL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of DVL3 BINDING SITE, designated SEQ ID:10700, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64230] Another function of VGAM1928 is therefore inhibition of Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM\_004423), a gene which regulates cell proliferation. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL3. The function of DVL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57.EGF-like-domain, Multiple 5 (EGFL5, Accession XM\_098838) is another VGAM1928 host target gene. EGFL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL5 BINDING SITE, designated SEQ ID:41884, to the nucleotide sequence of VGAM1928 RNA,

herein designated VGAM RNA, also designated SEQ ID:4639.

[64231] Another function of VGAM1928 is therefore inhibition of EGF-like-domain, Multiple 5 (EGFL5, Accession XM\_098838). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL5. Epithelial Membrane Protein 1 (EMP1, Accession NM\_001423) is another VGAM1928 host target gene. EMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EMP1 BINDING SITE, designated SEQ ID:7132, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64232] Another function of VGAM1928 is therefore inhibition of Epithelial Membrane Protein 1 (EMP1, Accession NM\_001423), a gene which plays a role in squamous cell differentiation; member of the PMP22/EMP/MP20 family of membrane glycoproteins. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with EMP1. The function of EMP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. Ectodermal-neural Cortex (with BTB-like domain) (ENC1, Accession NM\_003633) is another VGAM1928 host target gene. ENC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENC1 BINDING SITE, designated SEQ ID:9700, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64233] Another function of VGAM1928 is therefore inhibition of Ectodermal-neural Cortex (with BTB-like domain) (ENC1, Accession NM\_003633), a gene which is an actin-binding protein involved in the regulation of neuronal process formation and in differentiation of neural crest cells. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENC1. The function of ENC1 and its association



with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM233. Epidermal Growth Factor Receptor Pathway Substrate 8 (EPS8, Accession NM\_004447) is another VGAM1928 host target gene. EPS8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPS8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPS8 BINDING SITE, designated SEQ ID:10742, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64234] Another function of VGAM1928 is therefore inhibition of Epidermal Growth Factor Receptor Pathway Substrate 8 (EPS8, Accession NM\_004447), a gene which has a role in normal and neoplastic cell proliferation; contains an SH3 motif. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPS8. The function of EPS8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1533. Exostoses

(multiple) 2 (EXT2, Accession NM\_000401) is another VGAM1928 host target gene. EXT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EXT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXT2 BINDING SITE, designated SEQ ID:5975, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64235] Another function of VGAM1928 is therefore inhibition of Exostoses (multiple) 2 (EXT2, Accession NM\_000401). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXT2. Exostoses (multiple)-like 1 (EXTL1, Accession NM\_004455) is another VGAM1928 host target gene. EXTL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EXTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL1 BINDING SITE, designated SEQ ID:10758, to the nucleotide sequence of VGAM1928 RNA,

herein designated VGAM RNA, also designated SEQ ID:4639.

[64236] Another function of VGAM1928 is therefore inhibition of Exostoses (multiple)-like 1 (EXTL1, Accession NM\_004455), a gene which probably contribute to the synthesis of heparan sulfate and heparin. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL1. The function of EXTL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM806. Fibulin 1 (FBLN1, Accession NM\_006485) is another VGAM1928 host target gene. FBLN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBLN1 BINDING SITE, designated SEQ ID:13211, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64237] Another function of VGAM1928 is therefore inhibition of

Fibulin 1 (FBLN1, Accession NM\_006485), a gene which secreted glycoprotein; has EGF-like repeats, similar to anaphylatoxins C3a, C4a, and C5a. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBLN1. The function of FBLN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1770. Fukuyama Type Congenital Muscular Dystrophy (fukutin) (FCMD, Accession NM\_006731) is another VGAM1928 host target gene. FCMD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FCMD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FCMD BINDING SITE, designated SEQ ID:13575, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64238] Another function of VGAM1928 is therefore inhibition of Fukuyama Type Congenital Muscular Dystrophy (fukutin) (FCMD, Accession NM\_006731). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FCMD. Filaggrin (FLG, Accession XM\_048104) is another VGAM1928 host target gene. FLG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLG BINDING SITE, designated SEQ ID:35108, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64239] Another function of VGAM1928 is therefore inhibition of Filaggrin (FLG, Accession XM\_048104), a gene which aggregates keratin intermediate filaments . Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLG. The function of FLG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM899. Filamin B, Beta (actin binding protein 278) (FLNB, Accession XM\_030806) is another VGAM1928 host target gene. FLNB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by FLNB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLNB BINDING SITE, designated SEQ ID:31146, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64240] Another function of VGAM1928 is therefore inhibition of Filamin B, Beta (actin binding protein 278) (FLNB, Accession XM\_030806), a gene which Filamin B, beta; binds actin, interacts with cytoplasmic domain of Ibalpha. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLNB. The function of FLNB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM416. Follistatin-like 1 (FSTL1, Accession NM\_007085) is another VGAM1928 host target gene. FSTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FSTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FSTL1 BINDING SITE, designated SEQ ID:13949, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64241] Another function of VGAM1928 is therefore inhibition of Follistatin-like 1 (FSTL1, Accession NM\_007085), a gene which may modulate the action of some growth factors on cell proliferation and differentiation. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FSTL1. The function of FSTL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM791. Galanin Receptor 1 (GALR1, Accession NM\_001480) is another VGAM1928 host target gene. GALR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALR1 BINDING SITE, designated SEQ ID:7217, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ

ID:4639.

[64242] Another function of VGAM1928 is therefore inhibition of Galanin Receptor 1 (GALR1, Accession NM\_001480), a gene which plays a role in regulating ion transport. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALR1. The function of GALR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1245. Gap Junction Protein, Beta 3, 31kDa (connexin 31) (GJB3, Accession NM\_024009) is another VGAM1928 host target gene. GJB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GJB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GJB3 BINDING SITE, designated SEQ ID:23443, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64243] Another function of VGAM1928 is therefore inhibition of Gap Junction Protein, Beta 3, 31kDa (connexin 31) (GJB3, Accession NM\_024009). Accordingly, utilities of



VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GJB3. Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 1 (GNAI1, Accession NM\_002069) is another VGAM1928 host target gene. GNAI1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GNAI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAI1 BINDING SITE, designated SEQ ID:7840, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64244] Another function of VGAM1928 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 1 (GNAI1, Accession NM\_002069), a gene which is involved as modulators or transducers in various transmembrane signaling systems. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAI1. The function of GNAI1 and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM57. Golgi Re-assembly Stacking Protein 1, 65kDa (GORASP1, Accession NM\_031899) is another VGAM1928 host target gene. GORASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GORASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GORASP1 BINDING SITE, designated SEQ ID:25645, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64245] Another function of VGAM1928 is therefore inhibition of Golgi Reassembly Stacking Protein 1, 65kDa (GORASP1, Accession NM\_031899), a gene which has some function with the Golgi apparatus. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GORASP1. The function of GORASP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM630. Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM\_085943) is an-

other VGAM1928 host target gene. GRLF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRLF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRLF1 BINDING SITE, designated SEQ ID:38412, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64246] Another function of VGAM1928 is therefore inhibition of Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM\_085943), a gene which inhibits transcription of the glucocorticoid receptor gene. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRLF1. The function of GRLF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.H3 Histone, Family 3B (H3.3B) (H3F3B, Accession NM\_005324) is another VGAM1928 host target gene. H3F3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H3F3B, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H3F3B BINDING SITE, designated SEQ ID:11796, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64247] Another function of VGAM1928 is therefore inhibition of H3 Histone, Family 3B (H3.3B) (H3F3B, Accession NM\_005324). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H3F3B. Huntingtin (Huntington disease) (HD, Accession NM\_002111) is another VGAM1928 host target gene. HD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HD BINDING SITE, designated SEQ ID:7893, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64248] Another function of VGAM1928 is therefore inhibition of Huntingtin (Huntington disease) (HD, Accession

NM\_002111). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HD. Heparan Sulfate (glucosamine) 3-O-sulfotransferase 3A1 (HS3ST3A1, Accession NM\_006042) is another VGAM1928 host target gene. HS3ST3A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HS3ST3A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS3ST3A1 BINDING SITE, designated SEQ ID:12678, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64249] Another function of VGAM1928 is therefore inhibition of Heparan Sulfate (glucosamine) 3-O-sulfotransferase 3A1 (HS3ST3A1, Accession NM\_006042), a gene which plays a role in the generation of heparan sulfate proteoglycan. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS3ST3A1. The function of HS3ST3A1 and its association with various diseases and clinical conditions, has been established by previous stud-

ies, as described hereinabove with reference to VGAM1454. Intercellular Adhesion Molecule 1 (CD54), Human Rhinovirus Receptor (ICAM1, Accession XM\_049518) is another VGAM1928 host target gene. ICAM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICAM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICAM1 BINDING SITE, designated SEQ ID:35441, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64250] Another function of VGAM1928 is therefore inhibition of Intercellular Adhesion Molecule 1 (CD54), Human Rhinovirus Receptor (ICAM1, Accession XM\_049518), a gene which binds the integrin LFA-1 (ITGB2) and promotes adhesion; member of the immunoglobulin superfamily. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICAM1. The function of ICAM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1677. Inhibitor of DNA

Binding 4, Dominant Negative Helix-loop-helix Protein (ID4, Accession NM\_001546) is another VGAM1928 host target gene. ID4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ID4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ID4 BINDING SITE, designated SEQ ID:7273, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64251] Another function of VGAM1928 is therefore inhibition of Inhibitor of DNA Binding 4, Dominant Negative Helix-loop-helix Protein (ID4, Accession NM\_001546), a gene which negatively regulates cell differentiation. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ID4. The function of ID4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM931. Isocitrate Dehydrogenase 1 (NADP+), Soluble (IDH1, Accession XM\_028869) is another VGAM1928 host target gene. IDH1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region

of mRNA encoded by IDH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IDH1 BINDING SITE, designated SEQ ID:30801, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64252] Another function of VGAM1928 is therefore inhibition of Isocitrate Dehydrogenase 1 (NADP+), Soluble (IDH1, Accession XM\_028869), a gene which decarboxylates isocitrate into alpha-ketoglutarate. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IDH1. The function of IDH1 has been established by previous studies. Henderson (1965) described electrophoretic polymorphism of this enzyme in mice. NADP-dependent IDH occurs in 2 structurally distinct forms: mitochondrial (OMIM Ref. No. 147650) and soluble (also called supernatant or cytoplasmic). Chen et al. (1972) found rare variants of the soluble form and concluded that the structural gene is probably autosomal and that it is distinct from the locus governing the mitochondrial form. Shows (1971) presented cell hybridization data suggesting that soluble



malate dehydrogenase and isocitrate dehydrogenase are syntenic. Using the cell-hybrid method which relies on interspecies variation rather than polymorphism, Boone et al. (1972) concluded that the IDH locus is on chromosome 20. The assignment of soluble IDH and soluble MDH (OMIM Ref. No. 154100) to chromosome 20 was withdrawn (Ruddle, 1973). Creagan et al. (1974) presented evidence that these 2 syntenic loci are on chromosome 2. From study of a balanced reciprocal translocation (X;2)(p22;q32) in man-mouse hybrids, Van Cong (1976) concluded that IDH1 is located in the region 2q32-qter. By dosage effect in cases of chromosome 2 aberrations, Narahara et al. (1985) concluded that the IDH1 locus is in 2q33.3, probably in the proximal portion. Glass et al. (1989) described a 16-year-old boy with deletion of the 2q32.2-q33.1 segment and normal levels of isocitrate dehydrogenase. Specific features included microphthalmia, corneal anomalies, beaked nose, ptosis, and cleft palate. In addition, the patient had a distinctive pattern of scalloped skin pigmentation, present from birth, which was approximately symmetrical on the trunk and proximal limbs and clearly demarcated from the normal skin. The distribution of pigmentation did not follow Blaschko lines.

There was no evidence of chromosomal mosaicism.

[64253] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64254] Glass, I. A.; Swindlehurst, C. A.; Aitken, D. A.; McCrea, W.; Boyd, E. : Interstitial deletion of the long arm of chromosome 2 with normal levels of isocitrate dehydrogenase. J. Med. Genet. 26: 127–130, 1989. ; and

[64255] Narahara, K.; Kimura, S.; Kikkawa, K.; Takahashi, Y.; Wakita, Y.; Kasai, R.; Nagai, S.; Nishibayashi, Y.; Kimoto, H. : Probable assignment of soluble isocitrate dehydrogenase (IDH–1) to.

[64256] Further studies establishing the function and utilities of IDH1 are found in John Hopkins OMIM database record ID 147700, and in cited publications numbered 5248–5260 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 11 (IL11, Accession NM\_000641) is another VGAM1928 host target gene. IL11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IL11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of IL11 BINDING SITE, designated SEQ ID:6279, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64257] Another function of VGAM1928 is therefore inhibition of Interleukin 11 (IL11, Accession NM\_000641), a gene which stimulates the proliferation of hematopoietic stem cells and megakaryocyte progenitor cells and induces megakaryocyte maturation. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL11. The function of IL11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Interleukin 13 Receptor, Alpha 1 (IL13RA1, Accession NM\_001560) is another VGAM1928 host target gene. IL13RA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL13RA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL13RA1 BINDING SITE, designated SEQ ID:7285, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ

ID:4639.

[64258] Another function of VGAM1928 is therefore inhibition of Interleukin 13 Receptor, Alpha 1 (IL13RA1, Accession NM\_001560), a gene which binds il-13 with a low affinity. together with il-4r- alpha can form a functional receptor for il-13. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL13RA1. The function of IL13RA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. Integrin, Beta 3 (platelet glycoprotein IIIa, antigen CD61) (ITGB3, Accession NM\_000212) is another VGAM1928 host target gene. ITGB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGB3 BINDING SITE, designated SEQ ID:5709, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64259] Another function of VGAM1928 is therefore inhibition of

Integrin, Beta 3 (platelet glycoprotein IIIa, antigen CD61) (ITGB3, Accession NM\_000212). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGB3. Intersectin 1 (SH3 domain protein) (ITSN1, Accession NM\_003024) is another VGAM1928 host target gene. ITSN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITSN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITSN1 BINDING SITE, designated SEQ ID:8956, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64260] Another function of VGAM1928 is therefore inhibition of Intersectin 1 (SH3 domain protein) (ITSN1, Accession NM\_003024), a gene which may be involved in endocytosis and synaptic vesicle recycling. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITSN1. The function of ITSN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM1233.Jerky Homolog (mouse) (JRK, Accession XM\_098818) is another VGAM1928 host target gene. JRK BINDING SITE1 and JRK BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by JRK, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JRK BINDING SITE1 and JRK BINDING SITE2, designated SEQ ID:41839 and SEQ ID:41840 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64261] Another function of VGAM1928 is therefore inhibition of Jerky Homolog (mouse) (JRK, Accession XM\_098818), a gene which might function as a DNA-binding protein. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JRK. The function of JRK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM210.Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 7 (KCNA7, Accession NM\_031886) is another VGAM1928

host target gene. KCNA7 BINDING SITE1 through KCNA7 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KCNA7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNA7 BINDING SITE1 through KCNA7 BINDING SITE4, designated SEQ ID:25627, SEQ ID:25629, SEQ ID:25630 and SEQ ID:25628 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64262] Another function of VGAM1928 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 7 (KCNA7, Accession NM\_031886), a gene which allows nerve cells to efficiently repolarize following an action potential. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNA7. The function of KCNA7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM126.V-maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog F (avian) (MAFF, Accession

NM\_012323) is another VGAM1928 host target gene.

MAFF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAFF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAFF BINDING SITE, designated SEQ ID:14700, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64263] Another function of VGAM1928 is therefore inhibition of V-maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog F (avian) (MAFF, Accession NM\_012323), a gene which Binds to the US-2 motif of the oxytocin receptor gene; has a leucine zipper structure. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAFF. The function of MAFF has been established by previous studies. Inoue et al. (1994) demonstrated that the US-2 element in the promoter of the human oxytocin receptor gene (OXTR; 167055) binds specifically nuclear proteins from human myometrium at parturition. Using the US-2 element in a yeast 1-hybrid system to screen a human myometrium cDNA library, Kimura et al. (1999)



isolated a full-length cDNA encoding the homolog of chicken MafF. Human MAFF encodes a deduced 164-amino acid protein with a predicted molecular mass of 17.8 kD. Like other small MAF proteins (e.g., MAFG, 602020), it contains an extended leucine zipper structure and lacks an N-terminal transactivating domain. Northern blot analysis showed a strong 2.6-kb signal in mRNA from term myometrium and from kidney, but not from non-pregnant myometrium. The MAFF protein is also preferentially expressed in term myometrium. The authors concluded that MAFF plays a role in OXTR gene upregulation at term.

[64264] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64265] Dunham, I.; Shimizu, N.; Roe, B. A.; Chissole, S.; Hunt, A. R.; Collins, J. E.; Bruskiewich, R.; Beare, D. M.; Clamp, M.; Smink, L. J.; Ainscough, R.; Almeida, J. P.; and 205 others : The DNA sequence of human chromosome 22. *Nature* 402: 489–495, 1999. ; and

[64266] Inoue, T.; Kimura, T.; Azuma, C.; Inazawa, J.; Takemura, M.; Kikuchi, T.; Kubota, Y.; Ogita, K.; Saji, F. : Structural organization of the human oxytocin receptor gene. *J. Biol.*

Chem. 2.

[64267] Further studies establishing the function and utilities of MAFF are found in John Hopkins OMIM database record ID 604877, and in cited publications numbered 675 and 6759 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Microtubule-associated Protein, RP/EB Family, Member 2 (MAPRE2, Accession NM\_014268) is another VGAM1928 host target gene. MAPRE2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPRE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE2 BINDING SITE, designated SEQ ID:15544, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64268] Another function of VGAM1928 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 2 (MAPRE2, Accession NM\_014268), a gene which The functional inactivation of the APC gene product is a key event in colorectal tumorigenesis. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MAPRE2. The function of MAPRE2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM\_012326) is another VGAM1928 host target gene. MAPRE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPRE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE3 BINDING SITE, designated SEQ ID:14716, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64269] Another function of VGAM1928 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM\_012326), a gene which interact with cytoplasmic microtubules, and with the adenomatous polyposis coli. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPRE3. The function of MAPRE3 and its association with various diseases and

clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340. Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM\_165540) is another VGAM1928 host target gene. MAT1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAT1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAT1A BINDING SITE, designated SEQ ID:43665, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64270] Another function of VGAM1928 is therefore inhibition of Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM\_165540). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAT1A. Mannosyl (alpha-1,3-)-glycoprotein Beta-1,2-N-acetylglucosaminyltransferase (MGAT1, Accession NM\_002406) is another VGAM1928 host target gene. MGAT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

MGAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGAT1 BINDING SITE, designated SEQ ID:8228, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64271] Another function of VGAM1928 is therefore inhibition of Mannosyl (alpha-1,3-)-glycoprotein Beta-1,2-N-acetylglucosaminyltransferase (MGAT1, Accession NM\_002406), a gene which exists as a single protein-encoding exon. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT1. The function of MGAT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM165.Meningioma Expressed Antigen 5 (hyaluronidase) (MGEA5, Accession NM\_012215) is another VGAM1928 host target gene. MGEA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGEA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGEA5 BINDING SITE, designated SEQ ID:14518, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64272] Another function of VGAM1928 is therefore inhibition of Meningioma Expressed Antigen 5 (hyaluronidase) (MGEA5, Accession NM\_012215), a gene which has a hyaluronidase activity. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGEA5. The function of MGEA5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM801.

Myotubularin Related Protein 8 (MTMR8, Accession NM\_015458) is another VGAM1928 host target gene. MTMR8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTMR8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR8 BINDING SITE, designated SEQ ID:17745, to the nucleotide sequence of VGAM1928 RNA,

herein designated VGAM RNA, also designated SEQ ID:4639.

[64273] Another function of VGAM1928 is therefore inhibition of Myotubularin Related Protein 8 (MTMR8, Accession NM\_015458), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTMR8. The function of MTMR8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM379. Nuclear Factor I/B (NFIB, Accession NM\_005596) is another VGAM1928 host target gene. NFIB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NFIB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFIB BINDING SITE, designated SEQ ID:12122, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64274] Another function of VGAM1928 is therefore inhibition of Nuclear Factor I/B (NFIB, Accession NM\_005596), a gene

which recognizes and binds the palindromic sequence 5'-ttggcnnnnngccaa-3' present in viral and cellular promoters. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFIB. The function of NFIB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM100.5'-nucleotidase, Cytosolic III (NT5C3, Accession NM\_016489) is another VGAM1928 host target gene. NT5C3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NT5C3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NT5C3 BINDING SITE, designated SEQ ID:18582, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64275] Another function of VGAM1928 is therefore inhibition of 5'-nucleotidase, Cytosolic III (NT5C3, Accession NM\_016489). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NT5C3. Oxidative-stress



Responsive 1 (OSR1, Accession NM\_005109) is another VGAM1928 host target gene. OSR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSR1 BINDING SITE, designated SEQ ID:11588, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64276] Another function of VGAM1928 is therefore inhibition of Oxidative-stress Responsive 1 (OSR1, Accession NM\_005109), a gene which mediates stress-activated signals. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSR1. The function of OSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM538. Paired Box Gene 5 (B-cell lineage specific activator protein) (PAX5, Accession NM\_016734) is another VGAM1928 host target gene. PAX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by PAX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAX5 BINDING SITE, designated SEQ ID:18789, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64277] Another function of VGAM1928 is therefore inhibition of Paired Box Gene 5 (B-cell lineage specific activator protein) (PAX5, Accession NM\_016734), a gene which plays a role in B-cell differentiation, neural development and spermatogenesis. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAX5. The function of PAX5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1151. Protocadherin 11 X-linked (PCDH11X, Accession NM\_032968) is another VGAM1928 host target gene. PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH11X, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING

SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2, designated SEQ ID:26789 and SEQ ID:26804 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64278] Another function of VGAM1928 is therefore inhibition of Protocadherin 11 X-linked (PCDH11X, Accession NM\_032968), a gene which is thought to play a fundamental role in cell-cell recognition essential for the segmental development and function of the central nervous system. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH11X. The function of PCDH11X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433. Phosphogluconate Dehydrogenase (PGD, Accession XM\_086151) is another VGAM1928 host target gene. PGD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PGD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of PGD BINDING SITE, designated SEQ ID:38522, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64279] Another function of VGAM1928 is therefore inhibition of Phosphogluconate Dehydrogenase (PGD, Accession XM\_086151), a gene which catalyzes a step in the pentose phosphate pathway, oxidates glucose-6-phosphate into 6-phosphoglucono-lactone. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PGD. The function of PGD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. Phosphoinositide-3-kinase, Catalytic, Gamma Polypeptide (PIK3CG, Accession NM\_002649) is another VGAM1928 host target gene. PIK3CG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3CG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3CG BINDING SITE, designated SEQ ID:8512, to the nu-

cleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64280] Another function of VGAM1928 is therefore inhibition of Phosphoinositide-3-kinase, Catalytic, Gamma Polypeptide (PIK3CG, Accession NM\_002649), a gene which regulating cell growth. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3CG. The function of PIK3CG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1389. Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM\_027982) is another VGAM1928 host target gene. PIK3R3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3R3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3R3 BINDING SITE, designated SEQ ID:30601, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64281] Another function of VGAM1928 is therefore inhibition of Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM\_027982). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3R3. Pleiomorphic Adenoma Gene-like 1 (PLAGL1, Accession NM\_002656) is another VGAM1928 host target gene. PLAGL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAGL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAGL1 BINDING SITE, designated SEQ ID:8528, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64282] Another function of VGAM1928 is therefore inhibition of Pleiomorphic Adenoma Gene-like 1 (PLAGL1, Accession NM\_002656), a gene which regulates apoptosis and cell cycle arrest. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAGL1. The function of PLAGL1 and its association with various diseases and clin-

ical conditions, has been established by previous studies, as described hereinabove with reference to VGAM89. Plexin A1 (PLXNA1, Accession XM\_051261) is another VGAM1928 host target gene. PLXNA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLXNA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLXNA1 BINDING SITE, designated SEQ ID:35790, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64283] Another function of VGAM1928 is therefore inhibition of Plexin A1 (PLXNA1, Accession XM\_051261). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLXNA1. Peanut-like 1 (Drosophila) (PNUTL1, Accession NM\_002688) is another VGAM1928 host target gene. PNUTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PNUTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of PNUTL1 BINDING SITE, designated SEQ ID:8547, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64284] Another function of VGAM1928 is therefore inhibition of Peanut-like 1 (Drosophila) (PNUTL1, Accession NM\_002688). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PNUTL1. Peptidylprolyl Isomerase (cyclophilin)-like 1 (PPIL1, Accession NM\_016059) is another VGAM1928 host target gene. PPIL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPIL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPIL1 BINDING SITE, designated SEQ ID:18133, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64285] Another function of VGAM1928 is therefore inhibition of Peptidylprolyl Isomerase (cyclophilin)-like 1 (PPIL1, Accession NM\_016059), a gene which catalyzes the cis-trans isomerization of proline imidic peptide bonds in



oligopeptides. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPIL1. The function of PPIL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1135. Protein Phosphatase 2, Regulatory Subunit B (B56), Epsilon Isoform (PPP2R5E, Accession NM\_006246) is another VGAM1928 host target gene. PPP2R5E BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPP2R5E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R5E BINDING SITE, designated SEQ ID:12922, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64286] Another function of VGAM1928 is therefore inhibition of Protein Phosphatase 2, Regulatory Subunit B (B56), Epsilon Isoform (PPP2R5E, Accession NM\_006246), a gene which is a regulatory subunit of protein phosphatase 2A. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with PPP2R5E. The function of PPP2R5E and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM302. PR Domain Containing 4 (PRDM4, Accession NM\_012406) is another VGAM1928 host target gene. PRDM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRDM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM4 BINDING SITE, designated SEQ ID:14784, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64287] Another function of VGAM1928 is therefore inhibition of PR Domain Containing 4 (PRDM4, Accession NM\_012406). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM4. PSA (Accession NM\_021154) is another VGAM1928 host target gene. PSA BINDING SITE1 and PSA BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PSA, corresponding to HOST TARGET binding sites such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSA BINDING SITE1 and PSA BINDING SITE2, designated SEQ ID:22132 and SEQ ID:27741 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64288] Another function of VGAM1928 is therefore inhibition of PSA (Accession NM\_021154), a gene which is puromycin-sensitive aminopeptidase and has metallopeptidase activity. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSA. The function of PSA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM65. Phosphatase and Tensin Homolog (mutated in multiple advanced cancers 1) (PTEN, Accession NM\_000314) is another VGAM1928 host target gene. PTEN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTEN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTEN BINDING SITE, designated SEQ

ID:5850, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64289] Another function of VGAM1928 is therefore inhibition of Phosphatase and Tensin Homolog (mutated in multiple advanced cancers 1) (PTEN, Accession NM\_000314). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTEN. Prostaglandin-endoperoxide Synthase 1 (prostaglandin G/H synthase and cyclooxygenase) (PTGS1, Accession NM\_000962) is another VGAM1928 host target gene. PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTGS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2, designated SEQ ID:6675 and SEQ ID:27896 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64290] Another function of VGAM1928 is therefore inhibition of Prostaglandin-endoperoxide Synthase 1 (prostaglandin G/

H synthase and cyclooxygenase) (PTGS1, Accession NM\_000962), a gene which may play an important role in regulating or promoting cell proliferation in some normal and neoplastically transformed cells. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGS1. The function of PTGS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. RAD17 Homolog (*S. pombe*) (RAD17, Accession NM\_002873) is another VGAM1928 host target gene. RAD17 BINDING SITE1 through RAD17 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD17, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD17 BINDING SITE1 through RAD17 BINDING SITE6, designated SEQ ID:8782, SEQ ID:28487, SEQ ID:28483, SEQ ID:28485, SEQ ID:28479 and SEQ ID:28489 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64291] Another function of VGAM1928 is therefore inhibition of RAD17 Homolog (*S. pombe*) (RAD17, Accession NM\_002873), a gene which may have a role in DNA damage-dependent and DNA replication-dependent cell cycle checkpoints. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD17. The function of RAD17 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM209. Regulatory Factor X-associated Protein (RFXAP, Accession NM\_000538) is another VGAM1928 host target gene. RFXAP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RFXAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFXAP BINDING SITE, designated SEQ ID:6135, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64292] Another function of VGAM1928 is therefore inhibition of Regulatory Factor X-associated Protein (RFXAP, Accession

NM\_000538), a gene which binds to the x-box of mhc ii promoters and is a transcriptional regulator. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFXAP. The function of RFXAP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM797. Regulator of G-protein Signalling 2, 24kDa (RGS2, Accession NM\_002923) is another VGAM1928 host target gene. RGS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS2 BINDING SITE, designated SEQ ID:8827, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64293] Another function of VGAM1928 is therefore inhibition of Regulator of G-protein Signalling 2, 24kDa (RGS2, Accession NM\_002923), a gene which inhibits signal transduction by increasing the gtpase activity of g protein thereby driving them into their inactive gdp-bound form. Accord-

ingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS2. The function of RGS2 has been established by previous studies. Genetic heterogeneity of Rieger syndrome has been suggested by the description of affected individuals with a variety of chromosomal abnormalities and by the report of failure to find linkage to 4q25 in 1 pedigree (Legius et al., 1994) Deletion of 13q14 was described in 2 cases (Akazawa et al., 1981; Stathacopoulos et al., 1987). Phillips et al. (1996) performed linkage analysis of a large 4 generation family and demonstrated that Rieger syndrome was not linked to 4q25 but to markers on 13q14. Phillips et al. (1996) pointed to forkhead (OMIM Ref. No. 136533) as an excellent candidate for the site of the mutation in this form of Rieger syndrome. They stated that if such mutations are found, this would be an example of a gene which can function both as an oncogene (producing rhabdomyosarcoma) and as a 'teratogene' (producing RIEG2).

[64294] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64295] Legius, E.; de Die-Smulders, C. E. M.; Verbraak, F.; Habex,



H.; Decorte, R.; Marynen, P.; Fryns, J. P.; Cassiman, J. J. : Genetic heterogeneity in Rieger eye malformation. J. Med. Genet. 31: 340–341, 1994. ; and

[64296] Phillips, J. C.; Del Bono, E. A.; Haines, J. L.; Pralea, A. M.; Cohen, J. S.; Greff, L. J.; Wiggs, J. L. : A second locus for Rieger syndrome maps to chromosome 13q14. Am. J. Hum. Genet. 59.

[64297] Further studies establishing the function and utilities of RGS2 are found in John Hopkins OMIM database record ID 601499, and in cited publications numbered 9486–326 and 9487 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ring Finger Protein 14 (RNF14, Accession NM\_004290) is another VGAM1928 host target gene. RNF14 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RNF14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF14 BINDING SITE, designated SEQ ID:10503, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64298] Another function of VGAM1928 is therefore inhibition of

Ring Finger Protein 14 (RNF14, Accession NM\_004290), a gene which associates with the androgen receptor (AR); functions as a transcriptional coactivator. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF14. The function of RNF14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827.RNA (guanine-7-) Methyltransferase (RNMT, Accession NM\_003799) is another VGAM1928 host target gene. RNMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNMT BINDING SITE, designated SEQ ID:9879, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64299] Another function of VGAM1928 is therefore inhibition of RNA (guanine-7-) Methyltransferase (RNMT, Accession NM\_003799), a gene which catalyzes the methylation of GpppN- at the guanine N7 position. Accordingly, utilities

of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNMT. The function of RNMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Arginyl Aminopeptidase (aminopeptidase B)-like 1 (RNPEPL1, Accession NM\_018226) is another VGAM1928 host target gene. RNPEPL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNPEPL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNPEPL1 BINDING SITE, designated SEQ ID:20163, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64300] Another function of VGAM1928 is therefore inhibition of Arginyl Aminopeptidase (aminopeptidase B)-like 1 (RNPEPL1, Accession NM\_018226). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNPEPL1. Retinitis Pigmentosa 2 (X-linked recessive) (RP2,

Accession NM\_006915) is another VGAM1928 host target gene. RP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP2 BINDING SITE, designated SEQ ID:13794, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64301] Another function of VGAM1928 is therefore inhibition of Retinitis Pigmentosa 2 (X-linked recessive) (RP2, Accession NM\_006915). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP2. Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754) is another VGAM1928 host target gene. RUNX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RUNX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RUNX1 BINDING SITE, designated SEQ ID:7501, to the nucleotide se-

quence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64302] Another function of VGAM1928 is therefore inhibition of Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RUNX1. Secreted Frizzled-related Protein 1 (SFRP1, Accession NM\_003012) is another VGAM1928 host target gene. SFRP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRP1 BINDING SITE, designated SEQ ID:8926, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64303] Another function of VGAM1928 is therefore inhibition of Secreted Frizzled-related Protein 1 (SFRP1, Accession NM\_003012), a gene which is a receptor for wnt proteins that may have an anti-apoptotic function. Accordingly, utilities of VGAM1928 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with SFRP1. The function of SFRP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM250. Splicing Factor, Arginine/serine-rich 7, 35kDa (SFRS7, Accession XM\_002575) is another VGAM1928 host target gene. SFRS7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRS7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS7 BINDING SITE, designated SEQ ID:29897, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64304] Another function of VGAM1928 is therefore inhibition of Splicing Factor, Arginine/serine-rich 7, 35kDa (SFRS7, Accession XM\_002575), a gene which is required for pre-mRNA splicing. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS7. The function of SFRS7 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM191.Surfactant, Pulmonary-associated Protein A2 (SFTPA2, Accession NM\_006926) is another VGAM1928 host target gene. SFTPA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFTPA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFTPA2 BINDING SITE, designated SEQ ID:13810, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64305] Another function of VGAM1928 is therefore inhibition of Surfactant, Pulmonary-associated Protein A2 (SFTPA2, Accession NM\_006926), a gene which plays a role in innate host defense in the lung. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFTPA2. The function of SFTPA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM148.Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member

3 (SLC11A3, Accession NM\_014585) is another VGAM1928 host target gene. SLC11A3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SLC11A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC11A3 BINDING SITE, designated SEQ ID:15942, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64306] Another function of VGAM1928 is therefore inhibition of Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 3 (SLC11A3, Accession NM\_014585). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC11A3. Solute Carrier Family 12 (potassium/chloride transporters), Member 7 (SLC12A7, Accession NM\_006598) is another VGAM1928 host target gene. SLC12A7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC12A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity



of the nucleotide sequences of SLC12A7 BINDING SITE, designated SEQ ID:13377, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64307] Another function of VGAM1928 is therefore inhibition of Solute Carrier Family 12 (potassium/chloride transporters), Member 7 (SLC12A7, Accession NM\_006598), a gene which is a potassium/chloride-cotransporter. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A7. The function of SLC12A7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Solute Carrier Family 19 (folate transporter), Member 1 (SLC19A1, Accession NM\_003056) is another VGAM1928 host target gene. SLC19A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC19A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC19A1 BINDING SITE, designated SEQ ID:9023, to the nucleotide sequence of VGAM1928 RNA,

herein designated VGAM RNA, also designated SEQ ID:4639.

[64308] Another function of VGAM1928 is therefore inhibition of Solute Carrier Family 19 (folate transporter), Member 1 (SLC19A1, Accession NM\_003056). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC19A1. Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM\_003043) is another VGAM1928 host target gene. SLC6A6 BINDING SITE1 and SLC6A6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC6A6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A6 BINDING SITE1 and SLC6A6 BINDING SITE2, designated SEQ ID:9006 and SEQ ID:9007 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64309] Another function of VGAM1928 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM\_003043), a gene

which transports taurine and other beta-amino acids like beta-alanine. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A6. The function of SLC6A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM36.SRP46 (Accession NM\_032102) is another VGAM1928 host target gene. SRP46 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRP46, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRP46 BINDING SITE, designated SEQ ID:25792, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64310] Another function of VGAM1928 is therefore inhibition of SRP46 (Accession NM\_032102). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRP46. Suppression of Tumorigenicity 7 (ST7, Accession NM\_021908) is another VGAM1928 host target gene. ST7

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ST7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST7 BINDING SITE, designated SEQ ID:22427, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64311] Another function of VGAM1928 is therefore inhibition of Suppression of Tumorigenicity 7 (ST7, Accession NM\_021908), a gene which has a role in regulating cell-environment or cell-cell interactions. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST7. The function of ST7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. Transcription Factor 19 (SC1) (TCF19, Accession XM\_175167) is another VGAM1928 host target gene. TCF19 BINDING SITE1 and TCF19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCF19, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF19 BINDING SITE1 and TCF19 BINDING SITE2, designated SEQ ID:46661 and SEQ ID:46710 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64312] Another function of VGAM1928 is therefore inhibition of Transcription Factor 19 (SC1) (TCF19, Accession XM\_175167), a gene which plays an important role in the transcription of genes required for the later stages of cell cycle progression. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF19. The function of TCF19 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM299.TH1-like (Drosophila) (TH1L, Accession NM\_016397) is another VGAM1928 host target gene. TH1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TH1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of TH1L BINDING SITE, designated SEQ ID:18536, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64313] Another function of VGAM1928 is therefore inhibition of TH1-like (Drosophila) (TH1L, Accession NM\_016397). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TH1L. Tissue Inhibitor of Metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory) (TIMP3, Accession NM\_000362) is another VGAM1928 host target gene. TIMP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TIMP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIMP3 BINDING SITE, designated SEQ ID:5927, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64314] Another function of VGAM1928 is therefore inhibition of Tissue Inhibitor of Metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory) (TIMP3, Accession NM\_000362). Accordingly, utilities of VGAM1928 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with TIMP3. Transmembrane Protein with EGF-like and Two Follistatin-like Domains 2 (TMEFF2, Accession NM\_016192) is another VGAM1928 host target gene. TMEFF2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TMEFF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMEFF2 BINDING SITE, designated SEQ ID:18285, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64315] Another function of VGAM1928 is therefore inhibition of Transmembrane Protein with EGF-like and Two Follistatin-like Domains 2 (TMEFF2, Accession NM\_016192), a gene which is a survival factor for hippocampal and mesencephalic neurons. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMEFF2. The function of TMEFF2 has been established by previous studies. Horie et al. (2000) detected strong Tmeff2 signals in most regions of the brain including regions of the olfactory bulb,

hippocampus, cerebellum, and substantia nigra. By Northern blot analysis with whole mouse embryos, Uchida et al. (1999) found that Tmeff2 expression was detectable by embryonic day 11 and increased by embryonic days 15–17. They also observed immunostaining of Tmeff2 in adult rat mesenchymal cells of the lamina propria and fibroblasts localized in lamina propria. Uchida et al. (1999) detected both membrane-bound and soluble TMEFF2 in analysis of A172 cells. Uchida et al. (1999) found that purified, soluble TMEFF2 stimulated ERBB4, but not ERBB2 (OMIM Ref. No. 164870) or ERBB3 (OMIM Ref. No. 190151), in gastric cancer cells. By treating fetal rat primary neuron cultures with a purified recombinant TMEFF2 protein fragment, Horie et al. (2000) observed that TMEFF2 promotes the survival of hippocampal and mesencephalic, but not cortical neurons in primary culture. Adenomas are the precursors of most colorectal cancers. Hyperplastic polyps have been linked to a subset of colorectal cancers showing DNA microsatellite instability. Using a strategy that isolates differentially methylated sequences from hyperplastic polyps and normal mucosa, Young et al. (2001) identified a 370-bp sequence containing the 5-prime untranslated region and the first exon of the TM-



EFF2 gene, which they called HPP1 (hyperplastic polyposis gene-1). They used rapid amplification of cDNA ends to isolate HPP1 from normal mucosa. Using RT-PCR, they found that HPP1 was expressed in 28 of 30 (93%) normal colonic samples but in only 7 of 30 (23%) colorectal cancers (P less than 0.001). The 5-prime region of HPP1 included a CpG island containing 49 CpG sites, of which 96% were found to be methylated by bisulfite sequencing of DNA from colonic tumor samples. In situ hybridization of HPP1 indicated that expression occurs in epithelial and stromal elements in normal mucosa but is silenced in both cell types in early colonic neoplasia. HPP1 is predicted to encode a transmembrane protein containing follistatin and epidermal growth factor-like domains. Silencing of HPP1 by methylation may increase the probability of neoplastic transformation.

[64316] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64317] Horie, M.; Mitsumoto, Y.; Kyushiki, H.; Kanemoto, N.; Watanabe, A.; Taniguchi, Y.; Nishino, N.; Okamoto, T.; Kondo, M.; Mori, T.; Noguchi, K.; Nakamura, Y.; Takahashi, E.; Tanigami, A. : Identification and characterization

of TMEFF2, a novel survival factor for hippocampal and mesencephalic neurons. Genomics 67: 146–152, 2000. ; and

[64318] Young, J.; Biden, K. G.; Simms, L. A.; Huggard, P.; Karatic, R.; Eyre, H. J.; Sutherland, G. R.; Herath, N.; Barker, M.; Anderson, G. J.; Fitzpatrick, D. R.; Ramm, G. A.; Jass, J. R.,.

[64319] Further studies establishing the function and utilities of TMEFF2 are found in John Hopkins OMIM database record ID 605734, and in cited publications numbered 6918–6920 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transmembrane Protein 1 (TMEM1, Accession NM\_003274) is another VGAM1928 host target gene. TMEM1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TMEM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMEM1 BINDING SITE, designated SEQ ID:9291, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64320] Another function of VGAM1928 is therefore inhibition of Transmembrane Protein 1 (TMEM1, Accession NM\_003274). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMEM1. Tropomodulin 2 (neuronal) (TMOD2, Accession NM\_014548) is another VGAM1928 host target gene. TMOD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TMOD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMOD2 BINDING SITE, designated SEQ ID:15861, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64321] Another function of VGAM1928 is therefore inhibition of Tropomodulin 2 (neuronal) (TMOD2, Accession NM\_014548), a gene which is an actin-capping protein for the slow-growing end of filamentous actin. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMOD2. The function of TMOD2 and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM791. Triosephosphate Isomerase 1 (TPI1, Accession NM\_000365) is another VGAM1928 host target gene. TPI1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TPI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPI1 BINDING SITE, designated SEQ ID:5936, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64322] Another function of VGAM1928 is therefore inhibition of Triosephosphate Isomerase 1 (TPI1, Accession NM\_000365). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPI1. Tripartite Motif-containing 37 (TRIM37, Accession NM\_015294) is another VGAM1928 host target gene. TRIM37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM37

BINDING SITE, designated SEQ ID:17619, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64323] Another function of VGAM1928 is therefore inhibition of Tripartite Motif-containing 37 (TRIM37, Accession NM\_015294). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM37. Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM\_004621) is another VGAM1928 host target gene. TRPC6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC6 BINDING SITE, designated SEQ ID:10971, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64324] Another function of VGAM1928 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM\_004621), a gene which has calcium channel activity. Accordingly, utilities of

VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC6. The function of TRPC6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Transient Receptor Potential Cation Channel, Subfamily M, Member 2 (TRPM2, Accession NM\_003307) is another VGAM1928 host target gene. TRPM2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM2 BINDING SITE, designated SEQ ID:9310, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64325] Another function of VGAM1928 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 2 (TRPM2, Accession NM\_003307), a gene which may be a calcium channel. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM2. The function of TRPM2 has been established by previous

studies. Perraud et al. (2001) demonstrated that a 350-amino acid protein, designated NUDT9 (OMIM Ref. No. 606022), and a homologous domain (NUDT9 homology domain) near the C terminus of the LTRPC2 putative cation channel both function as specific ADP-ribose pyrophosphatases. Whole-cell and single-channel analysis of HEK293 cells expressing LTRPC2 showed that LTRPC2 functions as a calcium-permeable cation channel that is specifically gated by free ADP-ribose. The expression of native LTRPC2 transcripts is detectable in many tissues, including the U937 monocyte cell line, in which ADP-ribose induces large cation currents that closely match those mediated by recombinant LTRPC2. Perraud et al. (2001) concluded that intracellular ADP-ribose regulates calcium entry into cells that express LTRPC2. Hara et al. (2002) reported that LTRPC2 is activated by micromolar levels of H<sub>2</sub>O<sub>2</sub> and agents that produce reactive oxygen/nitrogen species. This sensitivity of LTRPC2 to redox state modifiers was attributable to an agonistic binding of beta-nicotinamide adenine dinucleotide to the MutT motif. Arachidonic acid and calcium were important positive regulators for LTRPC2. Heterologous LTRPC2 expression conferred susceptibility to death on HEK cells. Antisense

oligonucleotide experiments revealed physiologic involvement of native LTRPC2 in H<sub>2</sub>O<sub>2</sub>- and TNF- $\alpha$  (OMIM Ref. No. 191160)-induced calcium influx and cell death. Thus, LTRPC2 represents an important intrinsic mechanism that mediates calcium and sodium overload in response to disturbance of redox state in cell death. Animal model experiments lend further support to the function of TRPM2.

[64326] It is appreciated that the abovementioned animal model for TRPM2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[64327] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64328] Perraud, A.-L.; Fleig, A.; Dunn, C. A.; Bagley, L. A.; Launay, P.; Schmitz, C.; Stokes, A. J.; Zhu, Q.; Bessman, M. J.; Penner, R.; Kinet, J.-P.; Scharenberg, A. M. : ADP-ribose gating of the calcium-permeable LTRPC2 channel revealed by Nudix motif homology. *Nature* 411: 595-599, 2001. ; and

[64329] Hara, Y.; Wakamori, M.; Ishii, M.; Maeno, E.; Nishida, M.; Yoshida, T.; Yamada, H.; Shimizu, S.; Mori, E.; Kudoh, J.; Shimizu, S.; Kurose, H.; Okada, Y.; Imoto, K.; Mori, Y. :



LTRPC2 Ca<sup>2+</sup>.

[64330] Further studies establishing the function and utilities of TRPM2 are found in John Hopkins OMIM database record ID 603749, and in cited publications numbered 7593–7598 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Trichorhinophalangeal Syndrome I (TRPS1, Accession NM\_014112) is another VGAM1928 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15350, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64331] Another function of VGAM1928 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM\_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1.

The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. WNT1 Inducible Signaling Pathway Protein 1 (WISP1, Accession NM\_003882) is another VGAM1928 host target gene. WISP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WISP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WISP1 BINDING SITE, designated SEQ ID:9961, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64332] Another function of VGAM1928 is therefore inhibition of WNT1 Inducible Signaling Pathway Protein 1 (WISP1, Accession NM\_003882), a gene which is a member of connective tissue growth factor family. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WISP1. The function of WISP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with refer-

ence to VGAM1656.Wingless-type MMTV Integration Site Family, Member 5B (WNT5B, Accession NM\_032642) is another VGAM1928 host target gene. WNT5B BINDING SITE1 and WNT5B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WNT5B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT5B BINDING SITE1 and WNT5B BINDING SITE2, designated SEQ ID:26359 and SEQ ID:25057 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64333] Another function of VGAM1928 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 5B (WNT5B, Accession NM\_032642), a gene which is the ligand for members of the frizzled family of seven trans-membrane receptors and may be a signaling molecule . Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT5B. The function of WNT5B has been established by previous studies. The WNT gene family consists of structurally related genes encoding secreted

signaling molecules that have been implicated in oncogenesis and in several developmental processes, including regulation of cell fate and patterning during embryogenesis. For general information about WNT genes, see WNT1 (OMIM Ref. No. 164820). Using degenerate PCR and cDNA library screening to search for new members of the mouse Wnt family, Gavin et al. (1990) identified Wnt5b. Northern blot analysis detected expression of Wnt5b in all tissues tested, with the exception of adult spleen. In situ hybridization, detected expression of Wnt5b at low levels throughout the embryo and fetus from 6.5 to 14.5 days postcoitum. By searching human genome draft sequence for mouse Wnt5a homologs, Saitoh and Katoh (2001) identified WNT5B. Using database searches and PCR techniques, they assembled a WNT5B cDNA sequence. WNT5B encodes a deduced 359-amino acid protein with an N-terminal signal peptide, 4 N-linked glycosylation sites, and conserved residues of the WNT family. The WNT5B protein shares 80% sequence identity with WNT5A (OMIM Ref. No. 164975). Using Northern blot analysis, Saitoh and Katoh (2001) detected expression of 2.8- and 2.4-kb WNT5B transcripts at moderate levels in adult prostate and fetal brain and at low levels in fetal lung, kidney,

adult liver, ovary, and small intestine. Using cDNA-PCR, the authors also detected WNT5B in gastric cancer and teratocarcinoma cell lines. Saitoh and Katoh (2001) determined that the WNT5B gene contains 4 exons and spans about 16 kb of genomic DNA. Exon-intron boundaries are conserved between WNT5B and WNT5A, suggesting that the 2 genes may have been generated by duplication of an ancestral gene.

[64334] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64335] Gavin, B. J.; McMahon, J. A.; McMahon, A. P. : Expression of multiple novel Wnt-1/int-1-related genes during fetal and adult mouse development. *Genes Dev.* 4: 2319-2332, 1990. ; and

[64336] Saitoh, T.; Katoh, M. : Molecular cloning and characterization of human WNT5B on chromosome 12p13.3 region. *Int. J. Oncol.* 19: 347-351, 2001.

[64337] Further studies establishing the function and utilities of WNT5B are found in John Hopkins OMIM database record ID 606361, and in cited publications numbered 12747 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zic Family Member

1 (odd-paired homolog, Drosophila) (ZIC1, Accession NM\_003412) is another VGAM1928 host target gene. ZIC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZIC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZIC1 BINDING SITE, designated SEQ ID:9449, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64338] Another function of VGAM1928 is therefore inhibition of Zic Family Member 1 (odd-paired homolog, Drosophila) (ZIC1, Accession NM\_003412), a gene which may play a role in cerebellar development. Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZIC1. The function of ZIC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381. Ankyrin Repeat and BTB (POZ) Domain Containing 1 (ABTB1, Accession NM\_032548) is another VGAM1928 host target gene. ABTB1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by ABTB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABTB1 BINDING SITE, designated SEQ ID:26273, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64339] Another function of VGAM1928 is therefore inhibition of Ankyrin Repeat and BTB (POZ) Domain Containing 1 (ABTB1, Accession NM\_032548). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABTB1. S-adenosylhomocysteine Hydrolase-like 1 (AHCYL1, Accession NM\_006621) is another VGAM1928 host target gene. AHCYL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AHCYL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AHCYL1 BINDING SITE, designated SEQ ID:13404, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64340] Another function of VGAM1928 is therefore inhibition of S-adenosylhomocysteine Hydrolase-like 1 (AHCYL1, Accession NM\_006621). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AHCYL1. Ras Homolog Gene Family, Member F (in filopodia) (ARHF, Accession NM\_019034) is another VGAM1928 host target gene. ARHF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHF BINDING SITE, designated SEQ ID:21120, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64341] Another function of VGAM1928 is therefore inhibition of Ras Homolog Gene Family, Member F (in filopodia) (ARHF, Accession NM\_019034). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHF. ARL8 (Accession XM\_167671) is another VGAM1928 host target gene. ARL8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded



by ARL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARL8 BINDING SITE, designated SEQ ID:44761, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64342] Another function of VGAM1928 is therefore inhibition of ARL8 (Accession XM\_167671). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARL8. ARNTL2 (Accession NM\_020183) is another VGAM1928 host target gene. ARNTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARNTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNTL2 BINDING SITE, designated SEQ ID:21419, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64343] Another function of VGAM1928 is therefore inhibition of ARNTL2 (Accession NM\_020183). Accordingly, utilities of

VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNTL2. Activating Transcription Factor 3 (ATF3, Accession NM\_004024) is another VGAM1928 host target gene. ATF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATF3 BINDING SITE, designated SEQ ID:10242, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64344] Another function of VGAM1928 is therefore inhibition of Activating Transcription Factor 3 (ATF3, Accession NM\_004024). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATF3. Butyrophilin, Subfamily 1, Member A1 (BTN1A1, Accession NM\_001732) is another VGAM1928 host target gene. BTN1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of BTN1A1 BINDING SITE, designated SEQ ID:7467, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64345] Another function of VGAM1928 is therefore inhibition of Butyrophilin, Subfamily 1, Member A1 (BTN1A1, Accession NM\_001732). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN1A1. Butyrophilin, Subfamily 2, Member A2 (BTN2A2, Accession NM\_006995) is another VGAM1928 host target gene. BTN2A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN2A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN2A2 BINDING SITE, designated SEQ ID:13861, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64346] Another function of VGAM1928 is therefore inhibition of Butyrophilin, Subfamily 2, Member A2 (BTN2A2, Accession NM\_006995). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with BTN2A2. Chromosome 11 Open Reading Frame 11 (C11orf11, Accession XM\_167769) is another VGAM1928 host target gene. C11orf11 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C11orf11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf11 BINDING SITE, designated SEQ ID:44785, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64347] Another function of VGAM1928 is therefore inhibition of Chromosome 11 Open Reading Frame 11 (C11orf11, Accession XM\_167769). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf11. Chromosome 20 Open Reading Frame 178 (C20orf178, Accession XM\_059282) is another VGAM1928 host target gene. C20orf178 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of C20orf178 BINDING SITE, designated SEQ ID:36936, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64348] Another function of VGAM1928 is therefore inhibition of Chromosome 20 Open Reading Frame 178 (C20orf178, Accession XM\_059282). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf178. Chromosome 20 Open Reading Frame 42 (C20orf42, Accession NM\_017671) is another VGAM1928 host target gene. C20orf42 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf42 BINDING SITE, designated SEQ ID:19215, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64349] Another function of VGAM1928 is therefore inhibition of Chromosome 20 Open Reading Frame 42 (C20orf42, Ac-

cession NM\_017671). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf42. Chromosome 20 Open Reading Frame 98 (C20orf98, Accession XM\_049398) is another VGAM1928 host target gene. C20orf98 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf98, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf98 BINDING SITE, designated SEQ ID:35412, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64350] Another function of VGAM1928 is therefore inhibition of Chromosome 20 Open Reading Frame 98 (C20orf98, Accession XM\_049398). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf98. Chromosome 21 Open Reading Frame 4 (C21orf4, Accession NM\_006134) is another VGAM1928 host target gene. C21orf4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

C21orf4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf4 BINDING SITE, designated SEQ ID:12775, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64351] Another function of VGAM1928 is therefore inhibition of Chromosome 21 Open Reading Frame 4 (C21orf4, Accession NM\_006134). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf4. Cell Adhesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM\_006614) is another VGAM1928 host target gene. CHL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHL1 BINDING SITE, designated SEQ ID:13391, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64352] Another function of VGAM1928 is therefore inhibition of Cell Adhesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM\_006614). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHL1. Chondrolectin (CHODL, Accession NM\_024944) is another VGAM1928 host target gene. CHODL BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CHODL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHODL BINDING SITE, designated SEQ ID:24491, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64353] Another function of VGAM1928 is therefore inhibition of Chondrolectin (CHODL, Accession NM\_024944). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHODL. CCR4-NOT Transcription Complex, Subunit 7 (CNOT7, Accession NM\_013354) is another VGAM1928 host target gene. CNOT7 BINDING SITE is



HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNOT7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT7 BINDING SITE, designated SEQ ID:15004, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64354] Another function of VGAM1928 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 7 (CNOT7, Accession NM\_013354). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT7. CXYorf1 (Accession XM\_088704) is another VGAM1928 host target gene. CXYorf1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CXYorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXYorf1 BINDING SITE, designated SEQ ID:39915, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64355] Another function of VGAM1928 is therefore inhibition of CXYorf1 (Accession XM\_088704). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXYorf1. D4ST-1 (Accession NM\_130468) is another VGAM1928 host target gene. D4ST-1 BINDING SITE1 and D4ST-1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by D4ST-1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D4ST-1 BINDING SITE1 and D4ST-1 BINDING SITE2, designated SEQ ID:28226 and SEQ ID:28229 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64356] Another function of VGAM1928 is therefore inhibition of D4ST-1 (Accession NM\_130468). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D4ST-1. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681) is another VGAM1928 host target gene. DDX34 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by DDX34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE, designated SEQ ID:16167, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64357] Another function of VGAM1928 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 37 (DDX37, Accession NM\_032656) is another VGAM1928 host target gene. DDX37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX37 BINDING SITE, designated SEQ ID:26390, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4639.

[64358] Another function of VGAM1928 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 37 (DDX37, Accession NM\_032656). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX37. DKFZP434C171 (Accession NM\_015621) is another VGAM1928 host target gene. DKFZP434C171 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP434C171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C171 BINDING SITE, designated SEQ ID:17882, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64359] Another function of VGAM1928 is therefore inhibition of DKFZP434C171 (Accession NM\_015621). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C171. DKFZP434H0820 (Accession XM\_033460) is another VGAM1928 host target gene. DK–

FZP434H0820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434H0820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434H0820 BINDING SITE, designated SEQ ID:31933, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64360] Another function of VGAM1928 is therefore inhibition of DKFZP434H0820 (Accession XM\_033460). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434H0820. DKFZp547G183 (Accession NM\_018705) is another VGAM1928 host target gene. DKFZp547G183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547G183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547G183 BINDING SITE, designated SEQ ID:20790, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4639.

[64361] Another function of VGAM1928 is therefore inhibition of DKFZp547G183 (Accession NM\_018705). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547G183. DKFZp547O146 (Accession NM\_020224) is another VGAM1928 host target gene. DKFZp547O146 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547O146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547O146 BINDING SITE, designated SEQ ID:21485, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64362] Another function of VGAM1928 is therefore inhibition of DKFZp547O146 (Accession NM\_020224). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547O146. DKFZP564C1940 (Accession NM\_014045) is another VGAM1928 host target gene. DKFZP564C1940 BINDING SITE is HOST TARGET binding site

found in the 5' untranslated region of mRNA encoded by DKFZP564C1940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564C1940 BINDING SITE, designated SEQ ID:15272, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64363] Another function of VGAM1928 is therefore inhibition of DKFZP564C1940 (Accession NM\_014045). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564C1940. DKFZp564K142 (Accession NM\_032121) is another VGAM1928 host target gene. DKFZp564K142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp564K142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp564K142 BINDING SITE, designated SEQ ID:25808, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64364] Another function of VGAM1928 is therefore inhibition of DKFZp564K142 (Accession NM\_032121). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp564K142. DKFZP566K023 (Accession NM\_015485) is another VGAM1928 host target gene. DKFZP566K023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566K023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566K023 BINDING SITE, designated SEQ ID:17757, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64365] Another function of VGAM1928 is therefore inhibition of DKFZP566K023 (Accession NM\_015485). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566K023. DKFZp761D221 (Accession NM\_032291) is another VGAM1928 host target gene. DKFZp761D221 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by



DKFZp761D221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761D221 BINDING SITE, designated SEQ ID:26060, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64366] Another function of VGAM1928 is therefore inhibition of DKFZp761D221 (Accession NM\_032291). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761D221. DKFZP761G1913 (Accession NM\_031474) is another VGAM1928 host target gene. DKFZP761G1913 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP761G1913, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP761G1913 BINDING SITE, designated SEQ ID:25546, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64367] Another function of VGAM1928 is therefore inhibition of

DKFZP761G1913 (Accession NM\_031474). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761G1913. DKFZp761N0624 (Accession NM\_032295) is another VGAM1928 host target gene. DKFZp761N0624 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761N0624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761N0624 BINDING SITE, designated SEQ ID:26075, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64368] Another function of VGAM1928 is therefore inhibition of DKFZp761N0624 (Accession NM\_032295). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761N0624. DKFZp762A227 (Accession NM\_017611) is another VGAM1928 host target gene. DKFZp762A227 BINDING SITE1 and DKFZp762A227 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZp762A227, corre-

sponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762A227 BINDING SITE1 and DKFZp762A227 BINDING SITE2, designated SEQ ID:19105 and SEQ ID:15316 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64369] Another function of VGAM1928 is therefore inhibition of DKFZp762A227 (Accession NM\_017611). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762A227. F-box Only Protein 27 (FBXO27, Accession XM\_059045) is another VGAM1928 host target gene. FBXO27 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO27 BINDING SITE, designated SEQ ID:36837, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64370] Another function of VGAM1928 is therefore inhibition of F-box Only Protein 27 (FBXO27, Accession XM\_059045). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO27. FLJ10458 (Accession NM\_018096) is another VGAM1928 host target gene. FLJ10458 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10458, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10458 BINDING SITE, designated SEQ ID:19865, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64371] Another function of VGAM1928 is therefore inhibition of FLJ10458 (Accession NM\_018096). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10458. FLJ10460 (Accession NM\_018097) is another VGAM1928 host target gene. FLJ10460 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10460, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10460 BINDING SITE, designated SEQ ID:19869, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64372] Another function of VGAM1928 is therefore inhibition of FLJ10460 (Accession NM\_018097). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10460. FLJ10468 (Accession NM\_018101) is another VGAM1928 host target gene. FLJ10468 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10468 BINDING SITE, designated SEQ ID:19874, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64373] Another function of VGAM1928 is therefore inhibition of FLJ10468 (Accession NM\_018101). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ10468. FLJ10830 (Accession NM\_018235) is another VGAM1928 host target gene. FLJ10830 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10830, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10830 BINDING SITE, designated SEQ ID:20182, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64374] Another function of VGAM1928 is therefore inhibition of FLJ10830 (Accession NM\_018235). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10830. FLJ10956 (Accession NM\_018283) is another VGAM1928 host target gene. FLJ10956 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10956, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10956 BINDING SITE, designated SEQ ID:20273, to the nucleotide

sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64375] Another function of VGAM1928 is therefore inhibition of FLJ10956 (Accession NM\_018283). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10956. FLJ11126 (Accession NM\_018332) is another VGAM1928 host target gene. FLJ11126 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11126, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11126 BINDING SITE, designated SEQ ID:20334, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64376] Another function of VGAM1928 is therefore inhibition of FLJ11126 (Accession NM\_018332). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11126. FLJ11136 (Accession NM\_018336) is another VGAM1928 host target gene. FLJ11136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ11136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11136 BINDING SITE, designated SEQ ID:20339, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64377] Another function of VGAM1928 is therefore inhibition of FLJ11136 (Accession NM\_018336). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11136. FLJ11186 (Accession NM\_018353) is another VGAM1928 host target gene. FLJ11186 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11186, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11186 BINDING SITE, designated SEQ ID:20367, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64378] Another function of VGAM1928 is therefore inhibition of FLJ11186 (Accession NM\_018353). Accordingly, utilities of



VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11186. FLJ11301 (Accession NM\_018385) is another VGAM1928 host target gene. FLJ11301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11301 BINDING SITE, designated SEQ ID:20417, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64379] Another function of VGAM1928 is therefore inhibition of FLJ11301 (Accession NM\_018385). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11301. FLJ11726 (Accession NM\_024971) is another VGAM1928 host target gene. FLJ11726 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11726, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11726

BINDING SITE, designated SEQ ID:24528, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64380] Another function of VGAM1928 is therefore inhibition of FLJ11726 (Accession NM\_024971). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11726. FLJ12122 (Accession NM\_024979) is another VGAM1928 host target gene. FLJ12122 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12122 BINDING SITE, designated SEQ ID:24540, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64381] Another function of VGAM1928 is therefore inhibition of FLJ12122 (Accession NM\_024979). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12122. FLJ12484 (Accession XM\_045681) is another VGAM1928 host target gene. FLJ12484 BINDING SITE1 and

FLJ12484 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ12484, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12484 BINDING SITE1 and FLJ12484 BINDING SITE2, designated SEQ ID:34521 and SEQ ID:23023 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64382] Another function of VGAM1928 is therefore inhibition of FLJ12484 (Accession XM\_045681). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12484. FLJ13241 (Accession NM\_025088) is another VGAM1928 host target gene. FLJ13241 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13241 BINDING SITE, designated SEQ ID:24709, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM

RNA, also designated SEQ ID:4639.

[64383] Another function of VGAM1928 is therefore inhibition of FLJ13241 (Accession NM\_025088). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13241. FLJ13912 (Accession NM\_022770) is another VGAM1928 host target gene. FLJ13912 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13912 BINDING SITE, designated SEQ ID:23028, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64384] Another function of VGAM1928 is therefore inhibition of FLJ13912 (Accession NM\_022770). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13912. FLJ14327 (Accession NM\_024912) is another VGAM1928 host target gene. FLJ14327 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14327, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14327 BINDING SITE, designated SEQ ID:24421, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64385] Another function of VGAM1928 is therefore inhibition of FLJ14327 (Accession NM\_024912). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14327. FLJ14490 (Accession NM\_032793) is another VGAM1928 host target gene. FLJ14490 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14490, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14490 BINDING SITE, designated SEQ ID:26546, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64386] Another function of VGAM1928 is therefore inhibition of FLJ14490 (Accession NM\_032793). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ14490. FLJ20069 (Accession NM\_017651) is another VGAM1928 host target gene. FLJ20069 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20069, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20069 BINDING SITE, designated SEQ ID:19156, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64387] Another function of VGAM1928 is therefore inhibition of FLJ20069 (Accession NM\_017651). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20069. FLJ20085 (Accession NM\_017660) is another VGAM1928 host target gene. FLJ20085 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20085, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20085 BINDING SITE, designated SEQ ID:19184, to the nucleotide

sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64388] Another function of VGAM1928 is therefore inhibition of FLJ20085 (Accession NM\_017660). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20085. FLJ20584 (Accession NM\_017891) is another VGAM1928 host target gene. FLJ20584 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20584, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20584 BINDING SITE, designated SEQ ID:19561, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64389] Another function of VGAM1928 is therefore inhibition of FLJ20584 (Accession NM\_017891). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20584. FLJ20666 (Accession NM\_017922) is another VGAM1928 host target gene. FLJ20666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ20666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20666 BINDING SITE, designated SEQ ID:19585, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64390] Another function of VGAM1928 is therefore inhibition of FLJ20666 (Accession NM\_017922). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20666. FLJ21324 (Accession XM\_165988) is another VGAM1928 host target gene. FLJ21324 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21324, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21324 BINDING SITE, designated SEQ ID:43830, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64391] Another function of VGAM1928 is therefore inhibition of FLJ21324 (Accession XM\_165988). Accordingly, utilities of



VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21324. FLJ21977 (Accession NM\_032213) is another VGAM1928 host target gene. FLJ21977 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21977 BINDING SITE, designated SEQ ID:25940, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64392] Another function of VGAM1928 is therefore inhibition of FLJ21977 (Accession NM\_032213). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21977. FLJ22202 (Accession NM\_024883) is another VGAM1928 host target gene. FLJ22202 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22202, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22202

BINDING SITE, designated SEQ ID:24335, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64393] Another function of VGAM1928 is therefore inhibition of FLJ22202 (Accession NM\_024883). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22202. FLJ22215 (Accession XM\_173021) is another VGAM1928 host target gene. FLJ22215 BINDING SITE1 and FLJ22215 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ22215, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22215 BINDING SITE1 and FLJ22215 BINDING SITE2, designated SEQ ID:46279 and SEQ ID:23116 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64394] Another function of VGAM1928 is therefore inhibition of FLJ22215 (Accession XM\_173021). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ22215. FLJ22494 (Accession NM\_024815) is another VGAM1928 host target gene. FLJ22494 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22494 BINDING SITE, designated SEQ ID:24202, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64395] Another function of VGAM1928 is therefore inhibition of FLJ22494 (Accession NM\_024815). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22494. FLJ22529 (Accession NM\_024789) is another VGAM1928 host target gene. FLJ22529 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22529 BINDING SITE, designated SEQ ID:24169, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM

RNA, also designated SEQ ID:4639.

[64396] Another function of VGAM1928 is therefore inhibition of FLJ22529 (Accession NM\_024789). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22529. FLJ22746 (Accession NM\_024785) is another VGAM1928 host target gene. FLJ22746 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22746, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22746 BINDING SITE, designated SEQ ID:24163, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64397] Another function of VGAM1928 is therefore inhibition of FLJ22746 (Accession NM\_024785). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22746. FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM\_054016) is another VGAM1928 host target gene. FUSIP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by FUSIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUSIP1 BINDING SITE, designated SEQ ID:27623, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64398] Another function of VGAM1928 is therefore inhibition of FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM\_054016). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUSIP1. GBL (Accession NM\_022372) is another VGAM1928 host target gene. GBL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GBL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GBL BINDING SITE, designated SEQ ID:22760, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64399] Another function of VGAM1928 is therefore inhibition of

GBL (Accession NM\_022372). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GBL. GEMIN7 (Accession NM\_024707) is another VGAM1928 host target gene. GEMIN7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GEMIN7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GEMIN7 BINDING SITE, designated SEQ ID:24024, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64400] Another function of VGAM1928 is therefore inhibition of GEMIN7 (Accession NM\_024707). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GEMIN7. Glutamine-fructose-6-phosphate Transaminase 1 (GFPT1, Accession NM\_002056) is another VGAM1928 host target gene. GFPT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFPT1 BINDING SITE, designated SEQ ID:7818, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64401] Another function of VGAM1928 is therefore inhibition of Glutamine-fructose-6-phosphate Transaminase 1 (GFPT1, Accession NM\_002056). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFPT1. G Protein Pathway Suppressor 2 (GPS2, Accession XM\_102749) is another VGAM1928 host target gene. GPS2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPS2 BINDING SITE, designated SEQ ID:42147, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64402] Another function of VGAM1928 is therefore inhibition of G Protein Pathway Suppressor 2 (GPS2, Accession XM\_102749). Accordingly, utilities of VGAM1928 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with GPT2. Glutamic Pyruvate Transaminase (alanine aminotransferase) 2 (GPT2, Accession NM\_133443) is another VGAM1928 host target gene. GPT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPT2 BINDING SITE, designated SEQ ID:28522, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64403] Another function of VGAM1928 is therefore inhibition of Glutamic Pyruvate Transaminase (alanine aminotransferase) 2 (GPT2, Accession NM\_133443). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPT2. Glutamate Receptor, Ionotropic, N-methyl-D-aspartate 3A (GRIN3A, Accession NM\_133445) is another VGAM1928 host target gene. GRIN3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRIN3A, corresponding to a HOST TARGET binding site such as BINDING



SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN3A BINDING SITE, designated SEQ ID:28530, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64404] Another function of VGAM1928 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl-D-aspartate 3A (GRIN3A, Accession NM\_133445). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIN3A. GRO2 (Accession XM\_003510) is another VGAM1928 host target gene. GRO2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRO2 BINDING SITE, designated SEQ ID:29937, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64405] Another function of VGAM1928 is therefore inhibition of GRO2 (Accession XM\_003510). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with GRO2. Hypermethylated In Cancer 2 (HIC2, Accession XM\_036937) is another VGAM1928 host target gene. HIC2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HIC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC2 BINDING SITE, designated SEQ ID:32523, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64406] Another function of VGAM1928 is therefore inhibition of Hypermethylated In Cancer 2 (HIC2, Accession XM\_036937). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC2. HSC3 (Accession NM\_145174) is another VGAM1928 host target gene. HSC3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HSC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSC3 BINDING SITE, designated SEQ ID:29734,

to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64407] Another function of VGAM1928 is therefore inhibition of HSC3 (Accession NM\_145174). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSC3. HSPC067 (Accession NM\_014158) is another VGAM1928 host target gene. HSPC067 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPC067, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC067 BINDING SITE, designated SEQ ID:15458, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64408] Another function of VGAM1928 is therefore inhibition of HSPC067 (Accession NM\_014158). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC067. HSPC073 (Accession NM\_014163) is another VGAM1928 host target gene. HSPC073 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by HSPC073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC073 BINDING SITE, designated SEQ ID:15461, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64409] Another function of VGAM1928 is therefore inhibition of HSPC073 (Accession NM\_014163). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC073. HSPC156 (Accession NM\_014178) is another VGAM1928 host target gene. HSPC156 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC156, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC156 BINDING SITE, designated SEQ ID:15464, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64410] Another function of VGAM1928 is therefore inhibition of HSPC156 (Accession NM\_014178). Accordingly, utilities of

VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC156. HUMZD58C02 (Accession XM\_086862) is another VGAM1928 host target gene. HUMZD58C02 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HUMZD58C02, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HUMZD58C02 BINDING SITE, designated SEQ ID:38930, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64411] Another function of VGAM1928 is therefore inhibition of HUMZD58C02 (Accession XM\_086862). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HUMZD58C02. IMAGE:4907098 (Accession XM\_166247) is another VGAM1928 host target gene. IMAGE:4907098 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IMAGE:4907098, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMAGE:4907098 BINDING SITE, designated SEQ ID:44058, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64412] Another function of VGAM1928 is therefore inhibition of IMAGE:4907098 (Accession XM\_166247). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMAGE:4907098. JDD1 (Accession XM\_032515) is another VGAM1928 host target gene. JDD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JDD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JDD1 BINDING SITE, designated SEQ ID:31669, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64413] Another function of VGAM1928 is therefore inhibition of JDD1 (Accession XM\_032515). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JDD1.

Potassium Voltage-gated Channel, Isk-related Family, Member 4 (KCNE4, Accession NM\_080671) is another VGAM1928 host target gene. KCNE4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNE4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNE4 BINDING SITE, designated SEQ ID:27969, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64414] Another function of VGAM1928 is therefore inhibition of Potassium Voltage-gated Channel, Isk-related Family, Member 4 (KCNE4, Accession NM\_080671). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNE4. KIAA0205 (Accession NM\_014873) is another VGAM1928 host target gene. KIAA0205 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0205 BINDING SITE, designated SEQ ID:17008, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64415] Another function of VGAM1928 is therefore inhibition of KIAA0205 (Accession NM\_014873). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0205. KIAA0323 (Accession XM\_032634) is another VGAM1928 host target gene. KIAA0323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0323 BINDING SITE, designated SEQ ID:31696, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64416] Another function of VGAM1928 is therefore inhibition of KIAA0323 (Accession XM\_032634). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0323. KIAA0332 (Accession XM\_031553) is another VGAM1928 host target gene. KIAA0332 BINDING SITE is



HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0332 BINDING SITE, designated SEQ ID:31418, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64417] Another function of VGAM1928 is therefore inhibition of KIAA0332 (Accession XM\_031553). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0332. KIAA0335 (Accession NM\_014803) is another VGAM1928 host target gene. KIAA0335 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0335 BINDING SITE, designated SEQ ID:16729, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64418] Another function of VGAM1928 is therefore inhibition of

KIAA0335 (Accession NM\_014803). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0335. KIAA0376 (Accession XM\_037759) is another VGAM1928 host target gene. KIAA0376 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0376, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0376 BINDING SITE, designated SEQ ID:32675, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64419] Another function of VGAM1928 is therefore inhibition of KIAA0376 (Accession XM\_037759). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0376. KIAA0450 (Accession NM\_014638) is another VGAM1928 host target gene. KIAA0450 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0450 BINDING SITE, designated SEQ ID:16030, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64420] Another function of VGAM1928 is therefore inhibition of KIAA0450 (Accession NM\_014638). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0450. KIAA0478 (Accession NM\_014870) is another VGAM1928 host target gene. KIAA0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0478 BINDING SITE, designated SEQ ID:16982, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64421] Another function of VGAM1928 is therefore inhibition of KIAA0478 (Accession NM\_014870). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0478. KIAA0495 (Accession XM\_031397) is another

VGAM1928 host target gene. KIAA0495 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0495 BINDING SITE, designated SEQ ID:31355, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64422] Another function of VGAM1928 is therefore inhibition of KIAA0495 (Accession XM\_031397). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0495. KIAA0514 (Accession NM\_014696) is another VGAM1928 host target gene. KIAA0514 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0514 BINDING SITE, designated SEQ ID:16203, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64423] Another function of VGAM1928 is therefore inhibition of KIAA0514 (Accession NM\_014696). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0514. KIAA0523 (Accession XM\_041964) is another VGAM1928 host target gene. KIAA0523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0523 BINDING SITE, designated SEQ ID:33648, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64424] Another function of VGAM1928 is therefore inhibition of KIAA0523 (Accession XM\_041964). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0523. KIAA0685 (Accession NM\_014678) is another VGAM1928 host target gene. KIAA0685 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0685, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0685 BINDING SITE, designated SEQ ID:16148, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64425] Another function of VGAM1928 is therefore inhibition of KIAA0685 (Accession NM\_014678). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0685. KIAA0720 (Accession XM\_030970) is another VGAM1928 host target gene. KIAA0720 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0720 BINDING SITE, designated SEQ ID:31235, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64426] Another function of VGAM1928 is therefore inhibition of KIAA0720 (Accession XM\_030970). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0720. KIAA0961 (Accession NM\_014898) is another VGAM1928 host target gene. KIAA0961 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0961 BINDING SITE, designated SEQ ID:17072, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64427] Another function of VGAM1928 is therefore inhibition of KIAA0961 (Accession NM\_014898). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0961. KIAA1001 (Accession NM\_014960) is another VGAM1928 host target gene. KIAA1001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1001 BINDING SITE, designated SEQ ID:17324, to the nucleotide sequence of VGAM1928 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4639.

[64428] Another function of VGAM1928 is therefore inhibition of KIAA1001 (Accession NM\_014960). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1001. KIAA1018 (Accession NM\_014967) is another VGAM1928 host target gene. KIAA1018 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1018 BINDING SITE, designated SEQ ID:17355, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64429] Another function of VGAM1928 is therefore inhibition of KIAA1018 (Accession NM\_014967). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1018. KIAA1023 (Accession NM\_017604) is another VGAM1928 host target gene. KIAA1023 BINDING SITE1 through KIAA1023 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded



by KIAA1023, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1023 BINDING SITE1 through KIAA1023 BINDING SITE3, designated SEQ ID:19097, SEQ ID:19095 and SEQ ID:19096 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64430] Another function of VGAM1928 is therefore inhibition of KIAA1023 (Accession NM\_017604). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1023. KIAA1036 (Accession NM\_014909) is another VGAM1928 host target gene. KIAA1036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1036 BINDING SITE, designated SEQ ID:17130, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64431] Another function of VGAM1928 is therefore inhibition of

KIAA1036 (Accession NM\_014909). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1036. KIAA1161 (Accession XM\_088501) is another VGAM1928 host target gene. KIAA1161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1161 BINDING SITE, designated SEQ ID:39747, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64432] Another function of VGAM1928 is therefore inhibition of KIAA1161 (Accession XM\_088501). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1161. KIAA1170 (Accession XM\_045907) is another VGAM1928 host target gene. KIAA1170 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1170 BINDING SITE, designated SEQ ID:34614, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64433] Another function of VGAM1928 is therefore inhibition of KIAA1170 (Accession XM\_045907). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1170. KIAA1183 (Accession XM\_031307) is another VGAM1928 host target gene. KIAA1183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1183 BINDING SITE, designated SEQ ID:31336, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64434] Another function of VGAM1928 is therefore inhibition of KIAA1183 (Accession XM\_031307). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1183. KIAA1233 (Accession XM\_032181) is another

VGAM1928 host target gene. KIAA1233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1233 BINDING SITE, designated SEQ ID:31592, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64435] Another function of VGAM1928 is therefore inhibition of KIAA1233 (Accession XM\_032181). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1233. KIAA1466 (Accession XM\_050285) is another VGAM1928 host target gene. KIAA1466 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1466 BINDING SITE, designated SEQ ID:35603, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64436] Another function of VGAM1928 is therefore inhibition of KIAA1466 (Accession XM\_050285). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1466. KIAA1656 (Accession XM\_038022) is another VGAM1928 host target gene. KIAA1656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1656 BINDING SITE, designated SEQ ID:32726, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64437] Another function of VGAM1928 is therefore inhibition of KIAA1656 (Accession XM\_038022). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1656. KIAA1691 (Accession XM\_166523) is another VGAM1928 host target gene. KIAA1691 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1691, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1691 BINDING SITE, designated SEQ ID:44463, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64438] Another function of VGAM1928 is therefore inhibition of KIAA1691 (Accession XM\_166523). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1691. KIAA1913 (Accession XM\_058167) is another VGAM1928 host target gene. KIAA1913 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1913, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1913 BINDING SITE, designated SEQ ID:36578, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64439] Another function of VGAM1928 is therefore inhibition of KIAA1913 (Accession XM\_058167). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1913. Lectin, Galactoside-binding, Soluble, 8 (galectin 8) (LGALS8, Accession NM\_006499) is another VGAM1928 host target gene. LGALS8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LGALS8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGALS8 BINDING SITE, designated SEQ ID:13246, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64440] Another function of VGAM1928 is therefore inhibition of Lectin, Galactoside-binding, Soluble, 8 (galectin 8) (LGALS8, Accession NM\_006499). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGALS8. LIN-28 (Accession NM\_024674) is another VGAM1928 host target gene. LIN-28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIN-28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIN-28 BIND-

ING SITE, designated SEQ ID:23982, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64441] Another function of VGAM1928 is therefore inhibition of LIN-28 (Accession NM\_024674). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIN-28. Methyl-CpG Binding Domain Protein 2 (MBD2, Accession NM\_015832) is another VGAM1928 host target gene. MBD2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MBD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBD2 BINDING SITE, designated SEQ ID:17945, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64442] Another function of VGAM1928 is therefore inhibition of Methyl-CpG Binding Domain Protein 2 (MBD2, Accession NM\_015832). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBD2. MGC10960 (Accession NM\_032653) is another VGAM1928 host target



gene. MGC10960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10960 BINDING SITE, designated SEQ ID:26382, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64443] Another function of VGAM1928 is therefore inhibition of MGC10960 (Accession NM\_032653). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10960. MGC20496 (Accession NM\_052845) is another VGAM1928 host target gene. MGC20496 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20496, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20496 BINDING SITE, designated SEQ ID:27424, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64444] Another function of VGAM1928 is therefore inhibition of MGC20496 (Accession NM\_052845). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20496. MGC2474 (Accession NM\_023931) is another VGAM1928 host target gene. MGC2474 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2474, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2474 BINDING SITE, designated SEQ ID:23419, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64445] Another function of VGAM1928 is therefore inhibition of MGC2474 (Accession NM\_023931). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2474. MGC2628 (Accession NM\_024076) is another VGAM1928 host target gene. MGC2628 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2628, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2628 BINDING SITE, designated SEQ ID:23510, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64446] Another function of VGAM1928 is therefore inhibition of MGC2628 (Accession NM\_024076). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2628. MGC26641 (Accession NM\_144971) is another VGAM1928 host target gene. MGC26641 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC26641, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC26641 BINDING SITE, designated SEQ ID:29585, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64447] Another function of VGAM1928 is therefore inhibition of MGC26641 (Accession NM\_144971). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC26641. MGC2752 (Accession XM\_085842) is another VGAM1928 host target gene. MGC2752 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2752, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2752 BINDING SITE, designated SEQ ID:38368, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64448] Another function of VGAM1928 is therefore inhibition of MGC2752 (Accession XM\_085842). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2752. MGC35521 (Accession NM\_145065) is another VGAM1928 host target gene. MGC35521 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC35521, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC35521 BINDING SITE, designated SEQ ID:29704, to the nucleotide sequence of VGAM1928 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4639.

[64449] Another function of VGAM1928 is therefore inhibition of MGC35521 (Accession NM\_145065). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC35521. MGC4677 (Accession NM\_052871) is another VGAM1928 host target gene. MGC4677 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4677, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4677 BINDING SITE, designated SEQ ID:27450, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64450] Another function of VGAM1928 is therefore inhibition of MGC4677 (Accession NM\_052871). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4677. MGC7036 (Accession NM\_145058) is another VGAM1928 host target gene. MGC7036 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC7036, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC7036 BINDING SITE, designated SEQ ID:29693, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64451] Another function of VGAM1928 is therefore inhibition of MGC7036 (Accession NM\_145058). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC7036. MGC9753 (Accession NM\_033419) is another VGAM1928 host target gene. MGC9753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC9753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC9753 BINDING SITE, designated SEQ ID:27246, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64452] Another function of VGAM1928 is therefore inhibition of MGC9753 (Accession NM\_033419). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC9753. MIG (Accession NM\_002416) is another VGAM1928 host target gene. MIG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MIG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIG BINDING SITE, designated SEQ ID:8250, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64453] Another function of VGAM1928 is therefore inhibition of MIG (Accession NM\_002416). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIG. Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM\_016622) is another VGAM1928 host target gene. MRPL35 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MRPL35, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL35 BINDING SITE, designated SEQ

ID:18736, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64454] Another function of VGAM1928 is therefore inhibition of Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM\_016622). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL35. Mitochondrial Ribosomal Protein S27 (MRPS27, Accession NM\_015084) is another VGAM1928 host target gene. MRPS27 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPS27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS27 BINDING SITE, designated SEQ ID:17474, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64455] Another function of VGAM1928 is therefore inhibition of Mitochondrial Ribosomal Protein S27 (MRPS27, Accession NM\_015084). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS27. Neuroblastoma,



Suppression of Tumorigenicity 1 (NBL1, Accession XM\_001434) is another VGAM1928 host target gene. NBL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NBL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NBL1 BINDING SITE, designated SEQ ID:29840, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64456] Another function of VGAM1928 is therefore inhibition of Neuroblastoma, Suppression of Tumorigenicity 1 (NBL1, Accession XM\_001434). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBL1. NCK Adaptor Protein 1 (NCK1, Accession NM\_006153) is another VGAM1928 host target gene. NCK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCK1 BINDING SITE, designated SEQ ID:12811, to the nucleotide se-

quence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64457] Another function of VGAM1928 is therefore inhibition of NCK Adaptor Protein 1 (NCK1, Accession NM\_006153). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCK1. NKX2C (Accession NM\_145285) is another VGAM1928 host target gene. NKX2C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NKX2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NKX2C BINDING SITE, designated SEQ ID:29802, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64458] Another function of VGAM1928 is therefore inhibition of NKX2C (Accession NM\_145285). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NKX2C. Obscurin, Cytoskeletal Calmodulin and Titin-interacting RhoGEF (OBSCN, Accession XM\_047536) is another

VGAM1928 host target gene. OBSCN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OBSCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OBSCN BINDING SITE, designated SEQ ID:34988, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64459] Another function of VGAM1928 is therefore inhibition of Obscurin, Cytoskeletal Calmodulin and Titin-interacting RhoGEF (OBSCN, Accession XM\_047536). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OBSCN. ORM1-like 2 (*S. cerevisiae*) (ORMDL2, Accession NM\_014182) is another VGAM1928 host target gene. ORMDL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ORMDL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ORMDL2 BINDING SITE, designated SEQ ID:15468, to the nucleotide sequence of VGAM1928 RNA,

herein designated VGAM RNA, also designated SEQ ID:4639.

[64460] Another function of VGAM1928 is therefore inhibition of ORM1-like 2 (*S. cerevisiae*) (ORMDL2, Accession NM\_014182). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ORMDL2. Oxysterol Binding Protein-like 8 (OSBPL8, Accession NM\_020841) is another VGAM1928 host target gene. OSBPL8 BINDING SITE1 and OSBPL8 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OSBPL8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL8 BINDING SITE1 and OSBPL8 BINDING SITE2, designated SEQ ID:21904 and SEQ ID:21905 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64461] Another function of VGAM1928 is therefore inhibition of Oxysterol Binding Protein-like 8 (OSBPL8, Accession NM\_020841). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with OSBPL8. Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession NM\_014644) is another VGAM1928 host target gene. PDE4DIP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PDE4DIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4DIP BINDING SITE, designated SEQ ID:16053, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64462] Another function of VGAM1928 is therefore inhibition of Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession NM\_014644). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4DIP. PEPP3 (Accession NM\_014935) is another VGAM1928 host target gene. PEPP3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PEPP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of PEPP3 BINDING SITE, designated SEQ ID:17237, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64463] Another function of VGAM1928 is therefore inhibition of PEPP3 (Accession NM\_014935). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEPP3. PIP3-E (Accession XM\_039749) is another VGAM1928 host target gene. PIP3-E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP3-E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP3-E BINDING SITE, designated SEQ ID:33183, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64464] Another function of VGAM1928 is therefore inhibition of PIP3-E (Accession XM\_039749). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP3-E. Protein-O-mannosyltransferase 1 (POMT1, Accession

NM\_007171) is another VGAM1928 host target gene. POMT1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by POMT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POMT1 BINDING SITE, designated SEQ ID:14017, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64465] Another function of VGAM1928 is therefore inhibition of Protein-O-mannosyltransferase 1 (POMT1, Accession NM\_007171). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POMT1. Protein Tyrosine Phosphatase, Receptor Type, F Polypeptide (PTPRF), Interacting Protein (liprin), Alpha 4 (PPFIA4, Accession XM\_046751) is another VGAM1928 host target gene. PPFIA4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPFIA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of PPFIA4 BINDING SITE, designated SEQ ID:34818, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64466] Another function of VGAM1928 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, F Polypeptide (PTPRF), Interacting Protein (liprin), Alpha 4 (PPFIA4, Accession XM\_046751). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPFIA4. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 14A (PPP1R14A, Accession NM\_033256) is another VGAM1928 host target gene. PPP1R14A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPP1R14A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R14A BINDING SITE, designated SEQ ID:27088, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64467] Another function of VGAM1928 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 14A



(PPP1R14A, Accession NM\_033256). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R14A. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM\_024607) is another VGAM1928 host target gene. PPP1R3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R3B BINDING SITE, designated SEQ ID:23854, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64468] Another function of VGAM1928 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM\_024607). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R3B. PRO0659 (Accession NM\_014138) is another VGAM1928 host target gene. PRO0659 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0659, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0659 BINDING SITE, designated SEQ ID:15408, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64469] Another function of VGAM1928 is therefore inhibition of PRO0659 (Accession NM\_014138). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0659. PRO1855 (Accession NM\_018509) is another VGAM1928 host target gene. PRO1855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1855 BINDING SITE, designated SEQ ID:20576, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64470] Another function of VGAM1928 is therefore inhibition of PRO1855 (Accession NM\_018509). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PRO1855. PRO2730 (Accession NM\_025222) is another VGAM1928 host target gene. PRO2730 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO2730, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2730 BINDING SITE, designated SEQ ID:24898, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64471] Another function of VGAM1928 is therefore inhibition of PRO2730 (Accession NM\_025222). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2730. RAB, Member of RAS Oncogene Family-like 4 (RABL4, Accession NM\_006860) is another VGAM1928 host target gene. RABL4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RABL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RABL4 BINDING SITE, des-

ignated SEQ ID:13728, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64472] Another function of VGAM1928 is therefore inhibition of RAB, Member of RAS Oncogene Family-like 4 (RABL4, Accession NM\_006860). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RABL4. Roundabout Homolog 4, Magic Roundabout (Drosophila) (ROBO4, Accession NM\_019055) is another VGAM1928 host target gene. ROBO4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ROBO4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROBO4 BINDING SITE, designated SEQ ID:21132, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64473] Another function of VGAM1928 is therefore inhibition of Roundabout Homolog 4, Magic Roundabout (Drosophila) (ROBO4, Accession NM\_019055). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ROBO4. RPP14 (Accession XM\_003044) is another VGAM1928 host target gene. RPP14 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RPP14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPP14 BINDING SITE, designated SEQ ID:29925, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64474] Another function of VGAM1928 is therefore inhibition of RPP14 (Accession XM\_003044). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPP14. SBB103 (Accession NM\_005785) is another VGAM1928 host target gene. SBB103 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SBB103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SBB103 BINDING SITE, designated SEQ ID:12366, to the nucleotide sequence of

VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64475] Another function of VGAM1928 is therefore inhibition of SBB103 (Accession NM\_005785). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SBB103. Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654) is another VGAM1928 host target gene. SDC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SDC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC3 BINDING SITE, designated SEQ ID:16076, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64476] Another function of VGAM1928 is therefore inhibition of Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC3. Syndecan Binding Protein (syntenin) (SDCBP, Accession NM\_005625) is another VGAM1928 host target gene. SDCBP BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by SDCBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDCBP BINDING SITE, designated SEQ ID:12136, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64477] Another function of VGAM1928 is therefore inhibition of Syndecan Binding Protein (syntenin) (SDCBP, Accession NM\_005625). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDCBP. Serologically Defined Colon Cancer Antigen 1 (SDCCAG1, Accession NM\_004713) is another VGAM1928 host target gene. SDCCAG1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SDCCAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDCCAG1 BINDING SITE, designated SEQ ID:11072, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ

ID:4639.

[64478] Another function of VGAM1928 is therefore inhibition of Serologically Defined Colon Cancer Antigen 1 (SDCCAG1, Accession NM\_004713). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SD-CCAG1. SES2 (Accession NM\_031459) is another VGAM1928 host target gene. SES2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SES2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SES2 BINDING SITE, designated SEQ ID:25481, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64479] Another function of VGAM1928 is therefore inhibition of SES2 (Accession NM\_031459). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SES2. SIPL (Accession NM\_018269) is another VGAM1928 host target gene. SIPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded



by SIPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIPL BINDING SITE, designated SEQ ID:20242, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64480] Another function of VGAM1928 is therefore inhibition of SIPL (Accession NM\_018269). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIPL. Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM\_000617) is another VGAM1928 host target gene. SLC11A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC11A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC11A2 BINDING SITE, designated SEQ ID:6225, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64481] Another function of VGAM1928 is therefore inhibition of Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM\_000617). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC11A2. SMC4 Structural Maintenance of Chromosomes 4-like 1 (yeast) (SMC4L1, Accession NM\_005496) is another VGAM1928 host target gene. SMC4L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMC4L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMC4L1 BINDING SITE, designated SEQ ID:12001, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64482] Another function of VGAM1928 is therefore inhibition of SMC4 Structural Maintenance of Chromosomes 4-like 1 (yeast) (SMC4L1, Accession NM\_005496). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMC4L1. Serine Palmitoyltransferase, Long Chain

Base Subunit 2 (SPTLC2, Accession NM\_004863) is another VGAM1928 host target gene. SPTLC2 BINDING SITE1 and SPTLC2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SPTLC2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTLC2 BINDING SITE1 and SPTLC2 BINDING SITE2, designated SEQ ID:11286 and SEQ ID:11285 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64483] Another function of VGAM1928 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM\_004863). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. Synaptotagmin XIII (SYT13, Accession XM\_167880) is another VGAM1928 host target gene. SYT13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of SYT13 BINDING SITE, designated SEQ ID:44888, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64484] Another function of VGAM1928 is therefore inhibition of Synaptotagmin XIII (SYT13, Accession XM\_167880). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYT13. TAF5-like RNA Polymerase II, P300/CBP-associated Factor (PCAF)-associated Factor, 65kDa (TAF5L, Accession NM\_014409) is another VGAM1928 host target gene. TAF5L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAF5L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF5L BINDING SITE, designated SEQ ID:15751, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64485] Another function of VGAM1928 is therefore inhibition of TAF5-like RNA Polymerase II, P300/CBP-associated Factor

(PCAF)-associated Factor, 65kDa (TAF5L, Accession NM\_014409). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF5L. TGFB-induced Factor 2 (TALE family homeobox) (TGIF2, Accession NM\_021809) is another VGAM1928 host target gene. TGIF2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TGIF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGIF2 BINDING SITE, designated SEQ ID:22364, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64486] Another function of VGAM1928 is therefore inhibition of TGFB-induced Factor 2 (TALE family homeobox) (TGIF2, Accession NM\_021809). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGIF2. Thioesterase, Adipose Associated (THEA, Accession XM\_038922) is another VGAM1928 host target gene. THEA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by THEA,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THEA BINDING SITE, designated SEQ ID:32949, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64487] Another function of VGAM1928 is therefore inhibition of Thioesterase, Adipose Associated (THEA, Accession XM\_038922). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THEA. Translocation Protein 1 (TLOC1, Accession NM\_003262) is another VGAM1928 host target gene. TLOC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TLOC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLOC1 BINDING SITE, designated SEQ ID:9274, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64488] Another function of VGAM1928 is therefore inhibition of Translocation Protein 1 (TLOC1, Accession NM\_003262).

Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLOC1. Trinucleotide Repeat Containing 5 (TNRC5, Accession NM\_006586) is another VGAM1928 host target gene. TNRC5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TNRC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNRC5 BINDING SITE, designated SEQ ID:13345, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64489] Another function of VGAM1928 is therefore inhibition of Trinucleotide Repeat Containing 5 (TNRC5, Accession NM\_006586). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNRC5. TNF Receptor-associated Factor 3 (TRAF3, Accession XM\_007256) is another VGAM1928 host target gene. TRAF3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRAF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAF3 BINDING SITE, designated SEQ ID:30041, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64490] Another function of VGAM1928 is therefore inhibition of TNF Receptor-associated Factor 3 (TRAF3, Accession XM\_007256). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF3. Tubby Homolog (mouse) (TUB, Accession NM\_003320) is another VGAM1928 host target gene. TUB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUB BINDING SITE, designated SEQ ID:9320, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64491] Another function of VGAM1928 is therefore inhibition of Tubby Homolog (mouse) (TUB, Accession NM\_003320). Accordingly, utilities of VGAM1928 include diagnosis,



prevention and treatment of diseases and clinical conditions associated with TUB. Yes-associated Protein 1, 65kDa (YAP1, Accession NM\_006106) is another VGAM1928 host target gene. YAP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by YAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YAP1 BINDING SITE, designated SEQ ID:12751, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64492] Another function of VGAM1928 is therefore inhibition of Yes-associated Protein 1, 65kDa (YAP1, Accession NM\_006106). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YAP1. Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM\_053023) is another VGAM1928 host target gene. ZFP91 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZFP91, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ZFP91 BINDING SITE, designated SEQ ID:27577, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64493] Another function of VGAM1928 is therefore inhibition of Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM\_053023). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP91. Zinc Finger Protein 304 (ZNF304, Accession NM\_020657) is another VGAM1928 host target gene. ZNF304 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF304, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF304 BINDING SITE, designated SEQ ID:21831, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64494] Another function of VGAM1928 is therefore inhibition of Zinc Finger Protein 304 (ZNF304, Accession NM\_020657). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with ZNF304. ZNF333 (Accession NM\_032433) is another VGAM1928 host target gene. ZNF333 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF333 BINDING SITE, designated SEQ ID:26203, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64495] Another function of VGAM1928 is therefore inhibition of ZNF333 (Accession NM\_032433). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF333. Zinc Finger Protein 33a (KOX 31) (ZNF33A, Accession XM\_166119) is another VGAM1928 host target gene. ZNF33A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF33A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF33A BINDING SITE, designated SEQ

ID:43900, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64496] Another function of VGAM1928 is therefore inhibition of Zinc Finger Protein 33a (KOX 31) (ZNF33A, Accession XM\_166119). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF33A. ZNF340 (Accession XM\_097701) is another VGAM1928 host target gene. ZNF340 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF340 BINDING SITE, designated SEQ ID:41035, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64497] Another function of VGAM1928 is therefore inhibition of ZNF340 (Accession XM\_097701). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF340. LOC115574 (Accession XM\_056240) is another

VGAM1928 host target gene. LOC115574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115574 BINDING SITE, designated SEQ ID:36368, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64498] Another function of VGAM1928 is therefore inhibition of LOC115574 (Accession XM\_056240). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115574. LOC116228 (Accession XM\_057659) is another VGAM1928 host target gene. LOC116228 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC116228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116228 BINDING SITE, designated SEQ ID:36535, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64499] Another function of VGAM1928 is therefore inhibition of LOC116228 (Accession XM\_057659). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116228. LOC124044 (Accession XM\_071871) is another VGAM1928 host target gene. LOC124044 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124044, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124044 BINDING SITE, designated SEQ ID:37430, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64500] Another function of VGAM1928 is therefore inhibition of LOC124044 (Accession XM\_071871). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124044. LOC126006 (Accession XM\_058956) is another VGAM1928 host target gene. LOC126006 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC126006, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126006 BINDING SITE, designated SEQ ID:36802, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64501] Another function of VGAM1928 is therefore inhibition of LOC126006 (Accession XM\_058956). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126006. LOC130497 (Accession XM\_059439) is another VGAM1928 host target gene. LOC130497 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130497 BINDING SITE, designated SEQ ID:36991, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64502] Another function of VGAM1928 is therefore inhibition of LOC130497 (Accession XM\_059439). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC130497. LOC130589 (Accession NM\_138801) is another VGAM1928 host target gene. LOC130589 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130589, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130589 BINDING SITE, designated SEQ ID:29022, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64503] Another function of VGAM1928 is therefore inhibition of LOC130589 (Accession NM\_138801). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130589. LOC130612 (Accession XM\_059461) is another VGAM1928 host target gene. LOC130612 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130612, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130612 BINDING SITE, designated SEQ ID:37000, to the nucleotide sequence of VGAM1928 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4639.

[64504] Another function of VGAM1928 is therefore inhibition of LOC130612 (Accession XM\_059461). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130612. LOC132299 (Accession XM\_059584) is another VGAM1928 host target gene. LOC132299 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC132299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132299 BINDING SITE, designated SEQ ID:37024, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64505] Another function of VGAM1928 is therefore inhibition of LOC132299 (Accession XM\_059584). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132299. LOC133362 (Accession XM\_068305) is another VGAM1928 host target gene. LOC133362 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC133362, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133362 BINDING SITE, designated SEQ ID:37378, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64506] Another function of VGAM1928 is therefore inhibition of LOC133362 (Accession XM\_068305). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133362. LOC137075 (Accession XM\_059895) is another VGAM1928 host target gene. LOC137075 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC137075, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC137075 BINDING SITE, designated SEQ ID:37102, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64507] Another function of VGAM1928 is therefore inhibition of LOC137075 (Accession XM\_059895). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC137075. LOC143286 (Accession XM\_096412) is another VGAM1928 host target gene. LOC143286 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC143286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143286 BINDING SITE, designated SEQ ID:40354, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64508] Another function of VGAM1928 is therefore inhibition of LOC143286 (Accession XM\_096412). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143286. LOC143677 (Accession XM\_096471) is another VGAM1928 host target gene. LOC143677 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC143677, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143677 BINDING SITE, designated SEQ ID:40372, to

the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64509] Another function of VGAM1928 is therefore inhibition of LOC143677 (Accession XM\_096471). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143677. LOC143916 (Accession XM\_084664) is another VGAM1928 host target gene. LOC143916 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143916 BINDING SITE, designated SEQ ID:37653, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64510] Another function of VGAM1928 is therefore inhibition of LOC143916 (Accession XM\_084664). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143916. LOC144058 (Accession XM\_084712) is another VGAM1928 host target gene. LOC144058 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC144058, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144058 BINDING SITE, designated SEQ ID:37675, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64511] Another function of VGAM1928 is therefore inhibition of LOC144058 (Accession XM\_084712). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144058. LOC144308 (Accession XM\_096575) is another VGAM1928 host target gene. LOC144308 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144308 BINDING SITE, designated SEQ ID:40406, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64512] Another function of VGAM1928 is therefore inhibition of LOC144308 (Accession XM\_096575). Accordingly, utilities

of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144308. LOC144453 (Accession XM\_084869) is another VGAM1928 host target gene. LOC144453 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144453 BINDING SITE, designated SEQ ID:37747, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64513] Another function of VGAM1928 is therefore inhibition of LOC144453 (Accession XM\_084869). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144453. LOC144486 (Accession XM\_096608) is another VGAM1928 host target gene. LOC144486 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC144486 BINDING SITE, designated SEQ ID:40417, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64514] Another function of VGAM1928 is therefore inhibition of LOC144486 (Accession XM\_096608). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144486. LOC144587 (Accession XM\_040195) is another VGAM1928 host target gene. LOC144587 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144587, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144587 BINDING SITE, designated SEQ ID:33269, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64515] Another function of VGAM1928 is therefore inhibition of LOC144587 (Accession XM\_040195). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144587. LOC144920 (Accession XM\_096688) is another VGAM1928 host target gene. LOC144920 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144920 BINDING SITE, designated SEQ ID:40466, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64516] Another function of VGAM1928 is therefore inhibition of LOC144920 (Accession XM\_096688). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144920. LOC145333 (Accession XM\_096766) is another VGAM1928 host target gene. LOC145333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145333 BINDING SITE, designated SEQ ID:40532, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64517] Another function of VGAM1928 is therefore inhibition of



LOC145333 (Accession XM\_096766). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145333. LOC145566 (Accession XM\_085174) is another VGAM1928 host target gene. LOC145566 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145566 BINDING SITE, designated SEQ ID:37899, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64518] Another function of VGAM1928 is therefore inhibition of LOC145566 (Accession XM\_085174). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145566. LOC145858 (Accession XM\_085258) is another VGAM1928 host target gene. LOC145858 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC145858 BINDING SITE, designated SEQ ID:38003, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64519] Another function of VGAM1928 is therefore inhibition of LOC145858 (Accession XM\_085258). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145858. LOC145899 (Accession XM\_096899) is another VGAM1928 host target gene. LOC145899 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145899, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145899 BINDING SITE, designated SEQ ID:40624, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64520] Another function of VGAM1928 is therefore inhibition of LOC145899 (Accession XM\_096899). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145899. LOC145942 (Accession XM\_085281) is an-

other VGAM1928 host target gene. LOC145942 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145942, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145942 BINDING SITE, designated SEQ ID:38015, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64521] Another function of VGAM1928 is therefore inhibition of LOC145942 (Accession XM\_085281). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145942. LOC145945 (Accession XM\_096908) is another VGAM1928 host target gene. LOC145945 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145945 BINDING SITE, designated SEQ ID:40633, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64522] Another function of VGAM1928 is therefore inhibition of LOC145945 (Accession XM\_096908). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC146224 (Accession XM\_085366) is another VGAM1928 host target gene. LOC146224 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146224 BINDING SITE, designated SEQ ID:38078, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64523] Another function of VGAM1928 is therefore inhibition of LOC146224 (Accession XM\_085366). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146224. LOC146603 (Accession XM\_085514) is another VGAM1928 host target gene. LOC146603 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146603, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146603 BINDING SITE, designated SEQ ID:38216, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64524] Another function of VGAM1928 is therefore inhibition of LOC146603 (Accession XM\_085514). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146603. LOC146669 (Accession XM\_085534) is another VGAM1928 host target gene. LOC146669 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146669 BINDING SITE, designated SEQ ID:38222, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64525] Another function of VGAM1928 is therefore inhibition of LOC146669 (Accession XM\_085534). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC146669. LOC147077 (Accession XM\_085699) is another VGAM1928 host target gene. LOC147077 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147077 BINDING SITE, designated SEQ ID:38293, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64526] Another function of VGAM1928 is therefore inhibition of LOC147077 (Accession XM\_085699). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147077. LOC147180 (Accession XM\_097207) is another VGAM1928 host target gene. LOC147180 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147180, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147180 BINDING SITE, designated SEQ ID:40816, to the nucleotide sequence of VGAM1928 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4639.

[64527] Another function of VGAM1928 is therefore inhibition of LOC147180 (Accession XM\_097207). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147180. LOC148113 (Accession XM\_086058) is another VGAM1928 host target gene. LOC148113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148113 BINDING SITE, designated SEQ ID:38473, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64528] Another function of VGAM1928 is therefore inhibition of LOC148113 (Accession XM\_086058). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148113. LOC148936 (Accession XM\_097556) is another VGAM1928 host target gene. LOC148936 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148936, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148936 BINDING SITE, designated SEQ ID:40934, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64529] Another function of VGAM1928 is therefore inhibition of LOC148936 (Accession XM\_097556). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148936. LOC148938 (Accession XM\_097555) is another VGAM1928 host target gene. LOC148938 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148938, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148938 BINDING SITE, designated SEQ ID:40927, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64530] Another function of VGAM1928 is therefore inhibition of LOC148938 (Accession XM\_097555). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC148938. LOC149692 (Accession XM\_097706) is another VGAM1928 host target gene. LOC149692 BINDING SITE1 and LOC149692 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC149692, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149692 BINDING SITE1 and LOC149692 BINDING SITE2, designated SEQ ID:41038 and SEQ ID:41039 respectively, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64531] Another function of VGAM1928 is therefore inhibition of LOC149692 (Accession XM\_097706). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149692. LOC150095 (Accession XM\_097805) is another VGAM1928 host target gene. LOC150095 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150095, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC150095 BINDING SITE, designated SEQ ID:41129, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64532] Another function of VGAM1928 is therefore inhibition of LOC150095 (Accession XM\_097805). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150095. LOC150271 (Accession XM\_097859) is another VGAM1928 host target gene. LOC150271 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41171, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64533] Another function of VGAM1928 is therefore inhibition of LOC150271 (Accession XM\_097859). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC150407 (Accession XM\_086906) is an-

other VGAM1928 host target gene. LOC150407 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150407 BINDING SITE, designated SEQ ID:38948, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64534] Another function of VGAM1928 is therefore inhibition of LOC150407 (Accession XM\_086906). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150407. LOC151176 (Accession XM\_098016) is another VGAM1928 host target gene. LOC151176 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151176, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151176 BINDING SITE, designated SEQ ID:41313, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64535] Another function of VGAM1928 is therefore inhibition of LOC151176 (Accession XM\_098016). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151176. LOC151571 (Accession XM\_098088) is another VGAM1928 host target gene. LOC151571 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151571, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151571 BINDING SITE, designated SEQ ID:41371, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64536] Another function of VGAM1928 is therefore inhibition of LOC151571 (Accession XM\_098088). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151571. LOC151959 (Accession XM\_098144) is another VGAM1928 host target gene. LOC151959 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151959, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151959 BINDING SITE, designated SEQ ID:41407, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64537] Another function of VGAM1928 is therefore inhibition of LOC151959 (Accession XM\_098144). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151959. LOC152185 (Accession NM\_144718) is another VGAM1928 host target gene. LOC152185 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152185, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152185 BINDING SITE, designated SEQ ID:29539, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64538] Another function of VGAM1928 is therefore inhibition of LOC152185 (Accession NM\_144718). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC152185. LOC154282 (Accession XM\_098505) is another VGAM1928 host target gene. LOC154282 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154282, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154282 BINDING SITE, designated SEQ ID:41700, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64539] Another function of VGAM1928 is therefore inhibition of LOC154282 (Accession XM\_098505). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154282. LOC154881 (Accession XM\_088063) is another VGAM1928 host target gene. LOC154881 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154881 BINDING SITE, designated SEQ ID:39501, to the nucleotide sequence of VGAM1928 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4639.

[64540] Another function of VGAM1928 is therefore inhibition of LOC154881 (Accession XM\_088063). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154881. LOC158177 (Accession XM\_088506) is another VGAM1928 host target gene. LOC158177 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158177 BINDING SITE, designated SEQ ID:39761, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64541] Another function of VGAM1928 is therefore inhibition of LOC158177 (Accession XM\_088506). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158177. LOC158969 (Accession XM\_088728) is another VGAM1928 host target gene. LOC158969 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158969, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158969 BINDING SITE, designated SEQ ID:39924, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64542] Another function of VGAM1928 is therefore inhibition of LOC158969 (Accession XM\_088728). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158969. LOC163682 (Accession XM\_099402) is another VGAM1928 host target gene. LOC163682 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163682 BINDING SITE, designated SEQ ID:42084, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64543] Another function of VGAM1928 is therefore inhibition of LOC163682 (Accession XM\_099402). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC163682. LOC197408 (Accession XM\_117031) is another VGAM1928 host target gene. LOC197408 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC197408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197408 BINDING SITE, designated SEQ ID:43208, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64544] Another function of VGAM1928 is therefore inhibition of LOC197408 (Accession XM\_117031). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197408. LOC199796 (Accession XM\_058994) is another VGAM1928 host target gene. LOC199796 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC199796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199796 BINDING SITE, designated SEQ ID:36807, to

the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64545] Another function of VGAM1928 is therefore inhibition of LOC199796 (Accession XM\_058994). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199796. LOC200609 (Accession XM\_117256) is another VGAM1928 host target gene. LOC200609 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43338, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64546] Another function of VGAM1928 is therefore inhibition of LOC200609 (Accession XM\_117256). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. LOC201164 (Accession XM\_113904) is another VGAM1928 host target gene. LOC201164 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC201164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201164 BINDING SITE, designated SEQ ID:42531, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64547] Another function of VGAM1928 is therefore inhibition of LOC201164 (Accession XM\_113904). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201164. LOC201181 (Accession XM\_113916) is another VGAM1928 host target gene. LOC201181 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201181 BINDING SITE, designated SEQ ID:42535, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64548] Another function of VGAM1928 is therefore inhibition of LOC201181 (Accession XM\_113916). Accordingly, utilities

of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201181. LOC201191 (Accession XM\_117058) is another VGAM1928 host target gene. LOC201191 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201191 BINDING SITE, designated SEQ ID:43215, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64549] Another function of VGAM1928 is therefore inhibition of LOC201191 (Accession XM\_117058). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201191. LOC201799 (Accession XM\_114380) is another VGAM1928 host target gene. LOC201799 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201799, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC201799 BINDING SITE, designated SEQ ID:42913, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64550] Another function of VGAM1928 is therefore inhibition of LOC201799 (Accession XM\_114380). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201799. LOC203292 (Accession XM\_117527) is another VGAM1928 host target gene. LOC203292 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203292 BINDING SITE, designated SEQ ID:43501, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64551] Another function of VGAM1928 is therefore inhibition of LOC203292 (Accession XM\_117527). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203292. LOC204970 (Accession XM\_114795) is another VGAM1928 host target gene. LOC204970 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204970 BINDING SITE, designated SEQ ID:43072, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64552] Another function of VGAM1928 is therefore inhibition of LOC204970 (Accession XM\_114795). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204970. LOC219649 (Accession XM\_167562) is another VGAM1928 host target gene. LOC219649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219649 BINDING SITE, designated SEQ ID:44668, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64553] Another function of VGAM1928 is therefore inhibition of

LOC219649 (Accession XM\_167562). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219649. LOC219654 (Accession XM\_166095) is another VGAM1928 host target gene. LOC219654 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219654, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219654 BINDING SITE, designated SEQ ID:43870, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64554] Another function of VGAM1928 is therefore inhibition of LOC219654 (Accession XM\_166095). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219654. LOC219690 (Accession XM\_167572) is another VGAM1928 host target gene. LOC219690 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219690, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC219690 BINDING SITE, designated SEQ ID:44706, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64555] Another function of VGAM1928 is therefore inhibition of LOC219690 (Accession XM\_167572). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219690. LOC219790 (Accession XM\_166124) is another VGAM1928 host target gene. LOC219790 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219790, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219790 BINDING SITE, designated SEQ ID:43906, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64556] Another function of VGAM1928 is therefore inhibition of LOC219790 (Accession XM\_166124). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219790. LOC219920 (Accession XM\_167787) is an-



other VGAM1928 host target gene. LOC219920 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219920 BINDING SITE, designated SEQ ID:44810, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64557] Another function of VGAM1928 is therefore inhibition of LOC219920 (Accession XM\_167787). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219920. LOC220038 (Accession XM\_166257) is another VGAM1928 host target gene. LOC220038 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220038 BINDING SITE, designated SEQ ID:44081, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64558] Another function of VGAM1928 is therefore inhibition of LOC220038 (Accession XM\_166257). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220038. LOC220763 (Accession XM\_055551) is another VGAM1928 host target gene. LOC220763 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220763 BINDING SITE, designated SEQ ID:36300, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64559] Another function of VGAM1928 is therefore inhibition of LOC220763 (Accession XM\_055551). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220763. LOC220766 (Accession XM\_165471) is another VGAM1928 host target gene. LOC220766 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220766, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220766 BINDING SITE, designated SEQ ID:43649, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64560] Another function of VGAM1928 is therefore inhibition of LOC220766 (Accession XM\_165471). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220766. LOC220776 (Accession XM\_043388) is another VGAM1928 host target gene. LOC220776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220776 BINDING SITE, designated SEQ ID:33938, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64561] Another function of VGAM1928 is therefore inhibition of LOC220776 (Accession XM\_043388). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC220776. LOC221431 (Accession XM\_166380) is another VGAM1928 host target gene. LOC221431 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221431, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221431 BINDING SITE, designated SEQ ID:44219, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64562] Another function of VGAM1928 is therefore inhibition of LOC221431 (Accession XM\_166380). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221431. LOC221810 (Accession XM\_168222) is another VGAM1928 host target gene. LOC221810 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221810, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221810 BINDING SITE, designated SEQ ID:45083, to the nucleotide sequence of VGAM1928 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4639.

[64563] Another function of VGAM1928 is therefore inhibition of LOC221810 (Accession XM\_168222). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221810. LOC222183 (Accession XM\_168436) is another VGAM1928 host target gene. LOC222183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222183 BINDING SITE, designated SEQ ID:45187, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64564] Another function of VGAM1928 is therefore inhibition of LOC222183 (Accession XM\_168436). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222183. LOC222256 (Accession XM\_168571) is another VGAM1928 host target gene. LOC222256 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222256, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222256 BINDING SITE, designated SEQ ID:45248, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64565] Another function of VGAM1928 is therefore inhibition of LOC222256 (Accession XM\_168571). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222256. LOC253296 (Accession XM\_170512) is another VGAM1928 host target gene. LOC253296 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253296 BINDING SITE, designated SEQ ID:45345, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64566] Another function of VGAM1928 is therefore inhibition of LOC253296 (Accession XM\_170512). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC253296. LOC253649 (Accession XM\_171211) is another VGAM1928 host target gene. LOC253649 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC253649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253649 BINDING SITE, designated SEQ ID:45999, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64567] Another function of VGAM1928 is therefore inhibition of LOC253649 (Accession XM\_171211). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253649. LOC253650 (Accession XM\_171210) is another VGAM1928 host target gene. LOC253650 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC253650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253650 BINDING SITE, designated SEQ ID:45997, to

the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64568] Another function of VGAM1928 is therefore inhibition of LOC253650 (Accession XM\_171210). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253650. LOC255042 (Accession XM\_170896) is another VGAM1928 host target gene. LOC255042 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255042 BINDING SITE, designated SEQ ID:45650, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64569] Another function of VGAM1928 is therefore inhibition of LOC255042 (Accession XM\_170896). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255042. LOC256306 (Accession XM\_172976) is another VGAM1928 host target gene. LOC256306 BINDING SITE is HOST TARGET binding site found in the 3' un-



translated region of mRNA encoded by LOC256306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256306 BINDING SITE, designated SEQ ID:46237, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64570] Another function of VGAM1928 is therefore inhibition of LOC256306 (Accession XM\_172976). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256306. LOC256905 (Accession XM\_173031) is another VGAM1928 host target gene. LOC256905 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256905, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256905 BINDING SITE, designated SEQ ID:46297, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64571] Another function of VGAM1928 is therefore inhibition of LOC256905 (Accession XM\_173031). Accordingly, utilities

of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256905. LOC256925 (Accession XM\_175065) is another VGAM1928 host target gene. LOC256925 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256925 BINDING SITE, designated SEQ ID:46610, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64572] Another function of VGAM1928 is therefore inhibition of LOC256925 (Accession XM\_175065). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256925. LOC256942 (Accession XM\_170544) is another VGAM1928 host target gene. LOC256942 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256942, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC256942 BINDING SITE, designated SEQ ID:45365, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64573] Another function of VGAM1928 is therefore inhibition of LOC256942 (Accession XM\_170544). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256942. LOC257408 (Accession XM\_171176) is another VGAM1928 host target gene. LOC257408 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257408 BINDING SITE, designated SEQ ID:45956, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64574] Another function of VGAM1928 is therefore inhibition of LOC257408 (Accession XM\_171176). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257408. LOC257570 (Accession XM\_175239) is another VGAM1928 host target gene. LOC257570 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257570, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257570 BINDING SITE, designated SEQ ID:46698, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64575] Another function of VGAM1928 is therefore inhibition of LOC257570 (Accession XM\_175239). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257570. LOC51157 (Accession NM\_016202) is another VGAM1928 host target gene. LOC51157 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51157 BINDING SITE, designated SEQ ID:18298, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64576] Another function of VGAM1928 is therefore inhibition of

LOC51157 (Accession NM\_016202). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51157. LOC51285 (Accession NM\_016563) is another VGAM1928 host target gene. LOC51285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51285 BINDING SITE, designated SEQ ID:18636, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64577] Another function of VGAM1928 is therefore inhibition of LOC51285 (Accession NM\_016563). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51285. LOC89890 (Accession XM\_026976) is another VGAM1928 host target gene. LOC89890 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89890, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC89890 BINDING SITE, designated SEQ ID:30381, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64578] Another function of VGAM1928 is therefore inhibition of LOC89890 (Accession XM\_026976). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89890. LOC90139 (Accession NM\_130783) is another VGAM1928 host target gene. LOC90139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90139 BINDING SITE, designated SEQ ID:28274, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64579] Another function of VGAM1928 is therefore inhibition of LOC90139 (Accession NM\_130783). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90139. LOC90499 (Accession XM\_032170) is another

VGAM1928 host target gene. LOC90499 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90499 BINDING SITE, designated SEQ ID:31582, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64580] Another function of VGAM1928 is therefore inhibition of LOC90499 (Accession XM\_032170). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90499. LOC91040 (Accession XM\_035641) is another VGAM1928 host target gene. LOC91040 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91040 BINDING SITE, designated SEQ ID:32325, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64581] Another function of VGAM1928 is therefore inhibition of LOC91040 (Accession XM\_035641). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91040. LOC91291 (Accession XM\_037478) is another VGAM1928 host target gene. LOC91291 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91291, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91291 BINDING SITE, designated SEQ ID:32631, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64582] Another function of VGAM1928 is therefore inhibition of LOC91291 (Accession XM\_037478). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91291. LOC91516 (Accession XM\_038924) is another VGAM1928 host target gene. LOC91516 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91516, corresponding to a HOST TARGET binding site such as BINDING SITE I,



BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91516 BINDING SITE, designated SEQ ID:32955, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64583] Another function of VGAM1928 is therefore inhibition of LOC91516 (Accession XM\_038924). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91516. LOC92078 (Accession XM\_042684) is another VGAM1928 host target gene. LOC92078 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92078 BINDING SITE, designated SEQ ID:33742, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64584] Another function of VGAM1928 is therefore inhibition of LOC92078 (Accession XM\_042684). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC92078. LOC92360 (Accession XM\_044589) is another VGAM1928 host target gene. LOC92360 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92360, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92360 BINDING SITE, designated SEQ ID:34239, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64585] Another function of VGAM1928 is therefore inhibition of LOC92360 (Accession XM\_044589). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92360. LOC93550 (Accession XM\_051999) is another VGAM1928 host target gene. LOC93550 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93550, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93550 BINDING SITE, designated SEQ ID:35933, to the nucleotide sequence of VGAM1928 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4639.

[64586] Another function of VGAM1928 is therefore inhibition of LOC93550 (Accession XM\_051999). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93550. LOC93622 (Accession NM\_138699) is another VGAM1928 host target gene. LOC93622 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93622 BINDING SITE, designated SEQ ID:28950, to the nucleotide sequence of VGAM1928 RNA, herein designated VGAM RNA, also designated SEQ ID:4639.

[64587] Another function of VGAM1928 is therefore inhibition of LOC93622 (Accession NM\_138699). Accordingly, utilities of VGAM1928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93622. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1929 (VGAM1929) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[64588] VGAM1929 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1929 was detected is described hereinabove with reference to Figs. 1–8.

[64589] VGAM1929 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian Hemorrhagic Fever Virus. VGAM1929 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[64590] VGAM1929 gene encodes a VGAM1929 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1929 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1929 precursor RNA is designated SEQ ID:1915, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1915 is located at position 11778 relative to the genome of Simian Hemorrhagic Fever Virus.

[64591] VGAM1929 precursor RNA folds onto itself, forming

VGAM1929 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[64592] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1929 folded precursor RNA into VGAM1929 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 87%) nucleotide sequence of VGAM1929 RNA is designated SEQ ID:4640, and is provided hereinbelow with reference to the sequence listing part.

[64593] VGAM1929 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1929 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1929 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[64594] VGAM1929 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1929 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1929 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1929 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1929 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[64595] The complementary binding of VGAM1929 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1929 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1929 host target RNA into VGAM1929 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[64596] It is appreciated that VGAM1929 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1929 host target genes. The mRNA of each one of this plurality of VGAM1929 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1929 RNA, herein designated VGAM RNA, and which when bound by VGAM1929 RNA causes inhibition of translation of respective one or more VGAM1929 host target proteins.

[64597] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1929 gene, herein designated VGAM GENE, on one or more VGAM1929 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[64598] It is yet further appreciated that a function of VGAM1929 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of viral infection by Simian Hemorrhagic Fever Virus. Specific functions, and accordingly utilities, of VGAM1929 correlate with, and may be deduced from, the identity of the host target genes which VGAM1929 binds



and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[64599] Nucleotide sequences of the VGAM1929 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1929 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1929 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1929 are further described hereinbelow with reference to Table 1.

[64600] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1929 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1929 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[64601] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1929 gene, herein designated VGAM is inhibition of expression of VGAM1929 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1929 correlate with, and may be deduced from, the identity of the target genes which VGAM1929 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[64602] Adenylate Cyclase 7 (ADCY7, Accession NM\_001114) is a VGAM1929 host target gene. ADCY7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ADCY7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY7 BINDING SITE, designated SEQ ID:6786, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64603] A function of VGAM1929 is therefore inhibition of Adenylate Cyclase 7 (ADCY7, Accession NM\_001114), a gene which this a membrane-bound,  $Ca^{2+}$ -inhibitable adenylyl cyclase. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY7. The function of ADCY7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM108. Adrenomedullin (ADM, Accession NM\_001124) is another VGAM1929 host target gene. ADM BINDING SITE is HOST TARGET binding site found in the 3` un-

translated region of mRNA encoded by ADM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADM BINDING SITE, designated SEQ ID:6794, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64604] Another function of VGAM1929 is therefore inhibition of Adrenomedullin (ADM, Accession NM\_001124), a gene which regulates blood pressure and heart rate. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADM. The function of ADM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM842. V-akt Murine Thymoma Viral Oncogene Homolog 1 (AKT1, Accession NM\_005163) is another VGAM1929 host target gene. AKT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKT1 BIND-

ING SITE, designated SEQ ID:11651, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64605] Another function of VGAM1929 is therefore inhibition of V-akt Murine Thymoma Viral Oncogene Homolog 1 (AKT1, Accession NM\_005163), a gene which Serine-threonine protein kinase. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKT1. The function of AKT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM188. Amyotrophic Lateral Sclerosis 2 (juvenile) (ALS2, Accession NM\_020919) is another VGAM1929 host target gene. ALS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALS2 BINDING SITE, designated SEQ ID:21929, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64606] Another function of VGAM1929 is therefore inhibition of

Amyotrophic Lateral Sclerosis 2 (juvenile) (ALS2, Accession NM\_020919). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALS2. Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM\_001282) is another VGAM1929 host target gene. AP2B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP2B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP2B1 BINDING SITE, designated SEQ ID:6957, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64607] Another function of VGAM1929 is therefore inhibition of Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM\_001282), a gene which links clathrin to receptors in coated vesicles. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP2B1. The function of AP2B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM1126. Amyloid Beta (A4) Precursor Protein-binding, Family A, Member 1 (X11) (APBA1, Accession XM\_046018) is another VGAM1929 host target gene. APBA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APBA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APBA1 BINDING SITE, designated SEQ ID:34646, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64608] Another function of VGAM1929 is therefore inhibition of Amyloid Beta (A4) Precursor Protein-binding, Family A, Member 1 (X11) (APBA1, Accession XM\_046018), a gene which stabilises APP and inhibits production of proteolytic APP fragments. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APBA1. The function of APBA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Rho Guanine Nucleotide Exchange Factor (GEF) 12 (ARHGEF12,

Accession NM\_015313) is another VGAM1929 host target gene. ARHGEF12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF12 BINDING SITE, designated SEQ ID:17631, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64609] Another function of VGAM1929 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 12 (ARHGEF12, Accession NM\_015313). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF12. Ataxia Telangiectasia Mutated (includes complementation groups A, C and D) (ATM, Accession NM\_138293) is another VGAM1929 host target gene. ATM BINDING SITE1 and ATM BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ATM, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of ATM BINDING SITE1 and ATM BINDING SITE2, designated SEQ ID:28707 and SEQ ID:28705 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64610] Another function of VGAM1929 is therefore inhibition of Ataxia Telangiectasia Mutated (includes complementation groups A, C and D) (ATM, Accession NM\_138293). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATM. ATPase, Na<sup>+</sup>/K<sup>+</sup> Transporting, Beta 2 Polypeptide (ATP1B2, Accession NM\_001678) is another VGAM1929 host target gene. ATP1B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP1B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1B2 BINDING SITE, designated SEQ ID:7394, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64611] Another function of VGAM1929 is therefore inhibition of ATPase, Na<sup>+</sup>/K<sup>+</sup> Transporting, Beta 2 Polypeptide



(ATP1B2, Accession NM\_001678), a gene which catalyzes the hydrolysis of ATP coupled with the exchange of Na<sup>+</sup>/K<sup>+</sup> ions across the plasma membrane. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1B2. The function of ATP1B2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. ATPase, H<sup>+</sup> Transporting, Lysosomal 70kDa, V1 Subunit A, Isoform 1 (ATP6V1A1, Accession NM\_001690) is another VGAM1929 host target gene. ATP6V1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP6V1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP6V1A1 BINDING SITE, designated SEQ ID:7409, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64612] Another function of VGAM1929 is therefore inhibition of ATPase, H<sup>+</sup> Transporting, Lysosomal 70kDa, V1 Subunit A, Isoform 1 (ATP6V1A1, Accession NM\_001690), a gene

which is responsible for acidifying a variety of intracellular compartments in eukaryotic cells. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP6V1A1. The function of ATP6V1A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827.ATPase, Cu++ Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM\_000052) is another VGAM1929 host target gene. ATP7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP7A BINDING SITE, designated SEQ ID:5496, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64613] Another function of VGAM1929 is therefore inhibition of ATPase, Cu++ Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM\_000052). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with ATP7A. UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM\_004776) is another VGAM1929 host target gene. B4GALT5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by B4GALT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT5 BINDING SITE, designated SEQ ID:11169, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64614] Another function of VGAM1929 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM\_004776). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT5. BCRP2 (Accession XM\_031102) is another VGAM1929 host target gene. BCRP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BCRP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of BCRP2 BINDING SITE, designated SEQ ID:31277, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64615] Another function of VGAM1929 is therefore inhibition of BCRP2 (Accession XM\_031102). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCRP2. 2,3-bisphosphoglycerate Mutase (BPGM, Accession NM\_001724) is another VGAM1929 host target gene. BPGM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BPGM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BPGM BINDING SITE, designated SEQ ID:7456, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64616] Another function of VGAM1929 is therefore inhibition of 2,3-bisphosphoglycerate Mutase (BPGM, Accession NM\_001724), a gene which plays a role in regulating hemoglobin oxygen affinity. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with BPGM. The function of BPGM has been established by previous studies. Chen et al. (1971) described a genetically determined electrophoretic variant of 2,3-diphosphoglycerate mutase in a Canadian Eskimo family. The findings in heterozygotes were consistent with the view that the protein is a dimer of 2 identical subunits. Scott and Wright (1982) found DPGM to be polymorphic in 4 Alaskan ethnic groups. Hemoglobin and hematocrit were elevated in all deficient persons. Thus, both hemolytic anemia and polycythemia have been observed with deficiency of DPGM. Rosa et al. (1973, 1978) showed that the DPGM and 2,3-bisphosphoglycerate phosphatase activities of red cells are due to a single enzyme, bisphosphoglycerate mutase (EC 5.4.2.4). Joulin et al. (1986) cloned and sequenced cDNA for human red cell 2,3-bisphosphoglycerate mutase (EC 2.7.5.4). They presented a revised amino acid sequence of human BPGM based on the nucleotide sequence data. BPGM shows some phosphoglycerate mutase activity (Sasaki et al., 1975); nevertheless, the major portion of PGAM activity in the red cells is expressed by PGAMA (OMIM Ref. No. 172250), a protein genetically distinct from BPGM but

structurally related to it. The PGAMA locus is situated on chromosome 10. Using a cDNA clone for human BPGM in in situ hybridization experiments, Joulin et al. (1987) and Barichard et al. (1987) mapped the BPGM gene to 7q22–q34. Joulin et al. (1988) isolated the 2,3–bisphosphoglycerate mutase gene from genomic libraries. By Southern blots and DNA sequencing, they determined that it extends over 22 kb and is composed of 2 introns and 3 exons. The second exon correlates with a functional subdomain of the protein. No GC–rich sequence or GC box was found in the 5–prime flanking region of the gene. Both amino acid and cDNA sequence studies show that DPGAM is homologous to PGAM (172250, 261670) (Joulin et al., 1986; Yanagawa et al., 1986).

[64617] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64618] Rosa, R.; Prehu, M.–O.; Beuzard, Y.; Rosa, J. : The first case of a complete deficiency of diphosphoglycerate mutase in human erythrocytes. J. Clin. Invest. 62: 907–915, 1978. ; and

[64619] Joulin, V.; Peduzzi, J.; Romeo, P.–H.; Rosa, R.; Valentin, C.;

Dubart, A.; Lapeyre, B.; Blouquit, Y.; Garel, M.-C.;  
Goossens, M.; Rosa, J.; Cohen-Solal, M. : Molecular  
cloning and sequen.

[64620] Further studies establishing the function and utilities of  
BPGM are found in John Hopkins OMIM database record ID  
222800, and in cited publications numbered 9987-9989,  
1841, 9990-9995, 92, 9996-9998, 378 and 9999-10002  
listed in the bibliography section hereinbelow, which are  
also hereby incorporated by reference. BTG Family, Mem-  
ber 2 (BTG2, Accession NM\_006763) is another  
VGAM1929 host target gene. BTG2 BINDING SITE is HOST  
TARGET binding site found in the 3' untranslated region  
of mRNA encoded by BTG2, corresponding to a HOST  
TARGET binding site such as BINDING SITE I, BINDING SITE  
II or BINDING SITE III. Table 2 illustrates the complemen-  
tarity of the nucleotide sequences of BTG2 BINDING SITE,  
designated SEQ ID:13627, to the nucleotide sequence of  
VGAM1929 RNA, herein designated VGAM RNA, also des-  
ignated SEQ ID:4640.

[64621] Another function of VGAM1929 is therefore inhibition of  
BTG Family, Member 2 (BTG2, Accession NM\_006763). Ac-  
cordingly, utilities of VGAM1929 include diagnosis, pre-  
vention and treatment of diseases and clinical conditions

associated with BTG2. Capping Protein (actin filament) Muscle Z-line, Alpha 1 (CAPZA1, Accession XM\_052116) is another VGAM1929 host target gene. CAPZA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPZA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPZA1 BINDING SITE, designated SEQ ID:35949, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64622] Another function of VGAM1929 is therefore inhibition of Capping Protein (actin filament) Muscle Z-line, Alpha 1 (CAPZA1, Accession XM\_052116), a gene which is alpha 1 subunit of actin filament capping protein; binds actin, has roles in cell motility and actin assembly. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPZA1. The function of CAPZA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM547. CD83 Antigen (activated B lymphocytes, immunoglobulin superfamily) (CD83, Acces-



sion NM\_004233) is another VGAM1929 host target gene. CD83 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD83, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD83 BINDING SITE, designated SEQ ID:10427, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64623] Another function of VGAM1929 is therefore inhibition of CD83 Antigen (activated B lymphocytes, immunoglobulin superfamily) (CD83, Accession NM\_004233), a gene which may play a significant role in antigen presentation or the cellular interactions that follow lymphocyte activation. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD83. The function of CD83 has been established by previous studies. Many cell surface molecules that regulate immune responses contain conserved structural features similar to those found in immunoglobulins. These molecules are presumed to have evolved from a common precursor and are members of a large superfamily. Many of them are involved in cell-cell adhesion and

signal transduction Using flow cytometric analysis, Scholler et al. (2001) showed that CD83 binds to monocytes but not lymphocytes and that the binding is enhanced by stress. Immunoprecipitation and immunoblot analysis indicated that CD83 binds to a 72-kD ligand containing sialic acid. Scholler et al. (2001) concluded that CD83 is an adhesion receptor belonging to the SIGLEC family (see OMIM Ref. No. 600751). Animal model experiments lend further support to the function of CD83. Fujimoto et al. (2002) found that CD4 (OMIM Ref. No. 186940)-positive T-cell generation requires engagement of CD83. Cd83  $-/-$  mice had a specific block in Cd4 single-positive thymocyte development without increased Cd4/Cd8 (see OMIM Ref. No. 186910) double-positive or Cd8 single-positive thymocytes. This resulted in a selective 75 to 90% reduction in peripheral Cd4-positive T cells, predominantly within the naive subset. Wildtype thymocytes and bone marrow stem cells failed to differentiate into mature Cd4-positive T cells when transferred into Cd83  $-/-$  mice, while Cd83  $-/-$  thymocytes and stem cells developed normally in wildtype mice. The authors concluded that CD83 expression represents an additional regulatory component for CD4-positive T-cell develop-

ment in the thymus

- [64624] It is appreciated that the abovementioned animal model for CD83 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.
- [64625] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [64626] Scholler, N.; Hayden-Ledbetter, M.; Hellstrom, K.-E.; Hellstrom, I.; Ledbetter, J. A. : CD83 is a sialic acid-binding Ig-like lectin (Siglec) adhesion receptor that binds monocytes and a subset of activated CD8(+) T cells. J. Immun. 166: 3865-3872, 2001. ; and
- [64627] Fujimoto, Y.; Tu, L.; Miller, A. S.; Bock, C.; Fujimoto, M.; Doyle, C.; Steeber, D. A.; Tedder, T. F. : CD83 expression influences CD4+ T cell development in the thymus. Cell 108: 755-76.
- [64628] Further studies establishing the function and utilities of CD83 are found in John Hopkins OMIM database record ID 604534, and in cited publications numbered 7090-7094, 742 and 7460-7461 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cadherin 1, Type 1, E-cadherin (epithelial) (CDH1,

Accession NM\_004360) is another VGAM1929 host target gene. CDH1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH1 BINDING SITE, designated SEQ ID:10564, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64629] Another function of VGAM1929 is therefore inhibition of Cadherin 1, Type 1, E-cadherin (epithelial) (CDH1, Accession NM\_004360). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH1. Cadherin 6, Type 2, K-cadherin (fetal kidney) (CDH6, Accession NM\_004932) is another VGAM1929 host target gene. CDH6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDH6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH6 BINDING SITE, designated SEQ ID:11379, to the nucleotide sequence of VGAM1929 RNA, herein

designated VGAM RNA, also designated SEQ ID:4640.

[64630] Another function of VGAM1929 is therefore inhibition of Cadherin 6, Type 2, K-cadherin (fetal kidney) (CDH6, Accession NM\_004932), a gene which is a calcium dependent cell adhesion protein. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH6. The function of CDH6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60.CERD4 (Accession NM\_012074) is another VGAM1929 host target gene. CERD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CERD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CERD4 BINDING SITE, designated SEQ ID:14346, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64631] Another function of VGAM1929 is therefore inhibition of CERD4 (Accession NM\_012074). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CERD4. Chromodomain Helicase DNA Binding Protein 2 (CHD2, Accession NM\_001271) is another VGAM1929 host target gene. CHD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHD2 BINDING SITE, designated SEQ ID:6935, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64632] Another function of VGAM1929 is therefore inhibition of Chromodomain Helicase DNA Binding Protein 2 (CHD2, Accession NM\_001271). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHD2. CIS4 (Accession NM\_004232) is another VGAM1929 host target gene. CIS4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CIS4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CIS4 BINDING SITE, designated SEQ

ID:10424, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64633] Another function of VGAM1929 is therefore inhibition of CIS4 (Accession NM\_004232). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CIS4. Chloride Channel 4 (CLCN4, Accession NM\_001830) is another VGAM1929 host target gene. CLCN4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CLCN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN4 BINDING SITE, designated SEQ ID:7575, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64634] Another function of VGAM1929 is therefore inhibition of Chloride Channel 4 (CLCN4, Accession NM\_001830), a gene which is regulation of cell volume; membrane potential stabilization, signal transduction and transepithelial transport. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with CLCN4. The function of CLCN4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM558. Chloride Channel 6 (CLCN6, Accession NM\_001286) is another VGAM1929 host target gene. CLCN6 BINDING SITE1 through CLCN6 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CLCN6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN6 BINDING SITE1 through CLCN6 BINDING SITE3, designated SEQ ID:6961, SEQ ID:22338 and SEQ ID:22343 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64635] Another function of VGAM1929 is therefore inhibition of Chloride Channel 6 (CLCN6, Accession NM\_001286), a gene which is a voltage-gated chloride channel. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCN6. The function of CLCN6 and its association with various diseases and clinical conditions, has



been established by previous studies, as described herein above with reference to VGAM599. Ceroid-lipofuscinosis, Neuronal 5 (CLN5, Accession NM\_006493) is another VGAM1929 host target gene. CLN5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN5 BINDING SITE, designated SEQ ID:13227, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64636] Another function of VGAM1929 is therefore inhibition of Ceroid-lipofuscinosis, Neuronal 5 (CLN5, Accession NM\_006493). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN5. Clock Homolog (mouse) (CLOCK, Accession NM\_004898) is another VGAM1929 host target gene. CLOCK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLOCK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of CLOCK BINDING SITE, designated SEQ ID:11332, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64637] Another function of VGAM1929 is therefore inhibition of Clock Homolog (mouse) (CLOCK, Accession NM\_004898). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLOCK. Calponin 2 (CNN2, Accession NM\_004368) is another VGAM1929 host target gene. CNN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNN2 BINDING SITE, designated SEQ ID:10585, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64638] Another function of VGAM1929 is therefore inhibition of Calponin 2 (CNN2, Accession NM\_004368), a gene which may be involved in the structural organization and/or anchorage of actin filaments. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CNN2. The function of CNN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1498. COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM\_078470) is another VGAM1929 host target gene. COX15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX15 BINDING SITE, designated SEQ ID:27795, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64639] Another function of VGAM1929 is therefore inhibition of COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM\_078470). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX15. Cytochrome B-561 (CYB561, Accession NM\_001915) is another VGAM1929 host target gene. CYB561 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by CYB561, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYB561 BINDING SITE, designated SEQ ID:7631, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64640] Another function of VGAM1929 is therefore inhibition of Cytochrome B-561 (CYB561, Accession NM\_001915), a gene which is a secretory vesicle-specific electron transport protein. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYB561. The function of CYB561 has been established by previous studies. Cytochrome b561 is a major transmembrane protein that is specific to catecholamine and neuropeptide secretory vesicles of the adrenal medulla, pituitary gland, and other neuroendocrine tissues. This 30-kD cytochrome is present in both the small synaptic vesicles and the large dense core vesicles (chromaffin granules) of the tissues. Its role is to supply reducing equivalents to 2 monooxygenases, dopamine beta-hydroxylase (OMIM Ref. No.

223360) in chromaffin granules and peptidylglycine alpha-amidating monooxygenase (OMIM Ref. No. 170270) in neurosecretory vesicles. The cytochrome fulfills this role by catalyzing the transfer of electrons from a cytoplasmic donor, ascorbate, across a phospholipid bilayer to the luminal acceptor, semidehydroascorbate, in the interior of the vesicles. The continuously regenerated ascorbate within these vesicles is the immediate donor for the monooxygenases within the neuroendocrine secretory vesicles. Thus, cytochrome b561 is a transmembrane electron channel. Srivastava (1995) showed that the human CYB561 gene contains 5 exons spanning approximately 11 kb. Northern blots showed highest expression in colon cancer lines, T-cell lymphomas and K-562 cells.

[64641] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64642] McBride, O. W.; Yi, H. F.; Srivastava, M. : The human cytochrome b561 gene (CYB561) is located at 17q11-qter. Genomics 21: 662-663, 1994. ; and

[64643] Srivastava, M. : Genomic structure and expression of the human gene encoding cytochrome b(561), an integral protein of the chromaffin granule membrane. J. Biol. Chem.

270: 22714–22720, 1.

[64644] Further studies establishing the function and utilities of CYB561 are found in John Hopkins OMIM database record ID 600019, and in cited publications numbered 8789–8790 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cytochrome P450, Subfamily IVA, Polypeptide 11 (CYP4A11, Accession NM\_000778) is another VGAM1929 host target gene. CYP4A11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP4A11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP4A11 BINDING SITE, designated SEQ ID:6419, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64645] Another function of VGAM1929 is therefore inhibition of Cytochrome P450, Subfamily IVA, Polypeptide 11 (CYP4A11, Accession NM\_000778), a gene which catalyzes the omega- and (omega-1)-hydroxylation of various fatty acids. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with CYP4A11. The function of CYP4A11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM798. Cytochrome P450, Subfamily VIII B (sterol 12- $\alpha$ -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM\_004391) is another VGAM1929 host target gene. CYP8B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP8B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP8B1 BINDING SITE, designated SEQ ID:10626, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64646] Another function of VGAM1929 is therefore inhibition of Cytochrome P450, Subfamily VIII B (sterol 12- $\alpha$ -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM\_004391), a gene which functions in bile acid biosynthesis. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP8B1. The function of

CYP8B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM923.Dachshund Homolog (Drosophila) (DACH, Accession NM\_080759) is another VGAM1929 host target gene. DACH BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DACH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DACH BINDING SITE, designated SEQ ID:28036, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64647] Another function of VGAM1929 is therefore inhibition of Dachshund Homolog (Drosophila) (DACH, Accession NM\_080759), a gene which regulates early progenitor cell proliferation during retinogenesis and pituitary development . Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DACH. The function of DACH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM260.DEAD/H



(Asp–Glu–Ala–Asp/His) Box Polypeptide 20, 103kDa (DDX20, Accession NM\_007204) is another VGAM1929 host target gene. DDX20 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DDX20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX20 BINDING SITE, designated SEQ ID:14068, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64648] Another function of VGAM1929 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 20, 103kDa (DDX20, Accession NM\_007204), a gene which interacts with SMN and is required for pre-mRNA splicing in the nucleus. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX20. The function of DDX20 has been established by previous studies. Using coimmunoprecipitation, gel filtration experiments, and in vitro protein–binding assays, Charroux et al. (1999) showed that DDX20 is in a complex with SMN, Gemin2 (SIP1; 602595), and several spliceosomal Sm proteins of

snRNPs. Using deletion mutants, they determined that the C-terminal domain of DDX20 mediates the interaction with SMN. They concluded that DDX20 may play an important role in spliceosomal snRNP biogenesis. Klappacher et al. (2002) described a mechanism in which induction of the ETS repressor METS (ETV3; 164873) links terminal differentiation to cell cycle arrest. Using macrophages as a model, they provided evidence that METS blocks RAS (OMIM Ref. No. 190020)-dependent proliferation without inhibiting RAS-dependent expression of cell type-specific genes by selectively replacing ETS activators on the promoters of cell cycle control genes. The antiproliferative effects of METS required its interaction with DP103. Functional interactions between the METS/DP103 complex and E2F (see OMIM Ref. No. 189971)/RB (see OMIM Ref. No. 180200) family proteins were also necessary for inhibition of cellular proliferation, suggesting a combinatorial code that directs permanent cell cycle exit during terminal differentiation.

[64649] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64650] Charroux, B.; Pellizzoni, L.; Perkinson, R. A.; Shevchenko,

A.; Mann, M.; Dreyfuss, G. : Gemin3: a novel DEAD box protein that interacts with SMN, the spinal muscular atrophy gene product, and is a component of gems. J. Cell Biol. 147: 1181–1193, 1999. ; and

[64651] Klappacher, G. W.; Lunyak, V. V.; Sykes, D. B.; Sawka-Verhelle, D.; Sage, J.; Brard, G.; Ngo, S. D.; Gangadharan, D.; Jacks, T.; Kamps, M. P.; Rose, D. W.; Rosenfeld, M. G. : An induced.

[64652] Further studies establishing the function and utilities of DDX20 are found in John Hopkins OMIM database record ID 606168, and in cited publications numbered 4108–410 and 3141 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 6 (RNA helicase, 54kDa) (DDX6, Accession NM\_004397) is another VGAM1929 host target gene. DDX6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DDX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX6 BINDING SITE, designated SEQ ID:10649, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also des–

ignated SEQ ID:4640.

[64653] Another function of VGAM1929 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 6 (RNA helicase, 54kDa) (DDX6, Accession NM\_004397), a gene which is putative RNA helicases. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX6. The function of DDX6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. Distal-less Homeobox 4 (DLX4, Accession NM\_138281) is another VGAM1929 host target gene. DLX4 BINDING SITE1 and DLX4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DLX4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLX4 BINDING SITE1 and DLX4 BINDING SITE2, designated SEQ ID:28695 and SEQ ID:7647 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64654] Another function of VGAM1929 is therefore inhibition of

Distal-less Homeobox 4 (DLX4, Accession NM\_138281), a gene which may regulate gene expression, morphogenesis, and differentiation. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLX4. The function of DLX4 has been established by previous studies. Using degenerate PCR, Nakamura et al. (1996) cloned a gene, which they referred to as DLX7, from human and mouse that may represent the mammalian ortholog of the newt gene NuHBox-5. They isolated a human cDNA predicting a 167-amino acid protein. The homeodomains of these genes are highly similar to those of all other vertebrate DLX genes, but there is divergence upstream of the homeodomain between the human and mouse DLX7 genes and between DLX7 and other DLX genes. They presented evidence that the mouse Dlx7 gene is alternatively spliced. By Northern blot analysis, Nakamura et al. (1996) found that DLX7 is expressed as a 2.3-kb transcript in several human cell lines. By fluorescence in situ hybridization (FISH), Nakamura et al. (1996) mapped DLX7 to 17q21.3-q22. They stated that the human DLX7 and DLX3 (OMIM Ref. No. 600525) genes are 10 kb apart and are arranged in a tail-to-tail tandem ori-

entation, similarly to that found in mouse. Using dual-color FISH, Nakamura et al. (1996) determined that human DLX7 and HOX9B (OMIM Ref. No. 142964) lie within 2 Mb of one another. Quinn et al. (1997) undertook a DNA binding site screen of a 32-week human placental cDNA library using a consensus homeodomain binding site as a probe. They claimed that this study represented the first library screen carried out to isolate homeo box genes from the human placenta. They found that 3 homeo box genes known to be expressed in embryo, HB24 (OMIM Ref. No. 142995), GAX (OMIM Ref. No. 600535), and MSX2 (OMIM Ref. No. 123101), are also expressed in the placenta. They also identified a novel homeo box gene, designated DLX4 by them, that showed 85% sequence identity with the homeodomain encoded by the *Drosophila* 'distal-less' gene. Using FISH, they assigned DLX4 to 17q21-q22. This placed DLX4 in the same region of chromosome 17 as a member of the distal-less family gene DLX3 (OMIM Ref. No. 600525) and the HOXB homeo box gene cluster (see OMIM Ref. No. HOXB1; 142968). DLX1 (OMIM Ref. No. 600029) and DLX2 (OMIM Ref. No. 126255) are closely linked on chromosome 2; DLX5 (OMIM Ref. No. 600028) and DLX6 (OMIM Ref. No. 600030) are closely linked on

chromosome 7. Thus, Quinn et al. (1997) predicted that DLX3 and DLX4 are closely linked and that they arose through gene duplication and divergence from a common ancestral precursor.

[64655] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64656] Morasso, M. I.; Yonescu, R.; Griffin, C. A.; Sargent, T. D. : Localization of human DLX8 to chromosome 17q21.3–q22 by fluorescence in situ hybridization. *Mammalian Genome* 8: 302–303, 1997. ; and

[64657] Nakamura, S.; Stock, D. W.; Wydner, K. L.; Bollekens, J. A.; Takeshita, K.; Nagai, B. M.; Chiba, S.; Kitamura, T.; Freeland, T. M.; Zhao, Z.; Minowada, J.; Lawrence, J. B.; Weiss, K. M.

[64658] Further studies establishing the function and utilities of DLX4 are found in John Hopkins OMIM database record ID 601911, and in cited publications numbered 913 and 9133 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Deoxyribonuclease I (DNASE1, Accession NM\_005223) is another VGAM1929 host target gene. DNASE1 BINDING SITE is HOST TARGET binding site found

in the 5` untranslated region of mRNA encoded by DNASE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNASE1 BINDING SITE, designated SEQ ID:11717, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64659] Another function of VGAM1929 is therefore inhibition of Deoxyribonuclease I (DNASE1, Accession NM\_005223), a gene which seems to be involved in cell death. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNASE1. The function of DNASE1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM492. Desmoplakin (DPI, DPII) (DSP, Accession NM\_004415) is another VGAM1929 host target gene. DSP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DSP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the



nucleotide sequences of DSP BINDING SITE, designated SEQ ID:10677, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64660] Another function of VGAM1929 is therefore inhibition of Desmoplakin (DPI, DPII) (DSP, Accession NM\_004415). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSP. Dual Specificity Phosphatase 6 (DUSP6, Accession XM\_038308) is another VGAM1929 host target gene. DUSP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DUSP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP6 BINDING SITE, designated SEQ ID:32811, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64661] Another function of VGAM1929 is therefore inhibition of Dual Specificity Phosphatase 6 (DUSP6, Accession XM\_038308), a gene which inactivates map kinases. Accordingly, utilities of VGAM1929 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with DUSP6. The function of DUSP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1763. Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM\_004423) is another VGAM1929 host target gene. DVL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DVL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVL3 BINDING SITE, designated SEQ ID:10695, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64662] Another function of VGAM1929 is therefore inhibition of Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM\_004423), a gene which regulates cell proliferation. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL3. The function of DVL3 and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM57. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 2 (DYRK2, Accession NM\_003583) is another VGAM1929 host target gene. DYRK2 BINDING SITE1 and DYRK2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DYRK2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK2 BINDING SITE1 and DYRK2 BINDING SITE2, designated SEQ ID:9632 and SEQ ID:13208 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64663] Another function of VGAM1929 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 2 (DYRK2, Accession NM\_003583). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK2. Ephrin-B1 (EFNB1, Accession NM\_004429) is another VGAM1929 host target gene. EFNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNB1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNB1 BINDING SITE, designated SEQ ID:10713, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64664] Another function of VGAM1929 is therefore inhibition of Ephrin-B1 (EFNB1, Accession NM\_004429), a gene which is a transmembrane ligand of Eph-related receptor tyrosine kinases, has a role in cell adhesion. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNB1. The function of EFNB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM390.EH-domain Containing 3 (EHD3, Accession NM\_014600) is another VGAM1929 host target gene. EHD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EHD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EHD3 BINDING SITE, designated SEQ ID:15958,

to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64665] Another function of VGAM1929 is therefore inhibition of EH-domain Containing 3 (EHD3, Accession NM\_014600). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EHD3. EH-domain Containing 4 (EHD4, Accession NM\_139265) is another VGAM1929 host target gene. EHD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EHD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EHD4 BINDING SITE, designated SEQ ID:29257, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64666] Another function of VGAM1929 is therefore inhibition of EH-domain Containing 4 (EHD4, Accession NM\_139265). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EHD4. Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM\_012199) is an-

other VGAM1929 host target gene. EIF2C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF2C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2C1 BINDING SITE, designated SEQ ID:14505, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64667] Another function of VGAM1929 is therefore inhibition of Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM\_012199), a gene which plays an important role in the eukaryotic peptide chain initiation process. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF2C1. The function of EIF2C1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM118. Eukaryotic Translation Initiation Factor 2, Subunit 3 Gamma, 52kDa (EIF2S3, Accession NM\_001415) is another VGAM1929 host target gene. EIF2S3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

EIF2S3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2S3 BINDING SITE, designated SEQ ID:7112, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64668] Another function of VGAM1929 is therefore inhibition of Eukaryotic Translation Initiation Factor 2, Subunit 3 Gamma, 52kDa (EIF2S3, Accession NM\_001415), a gene which functions in the early steps of protein synthesis. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF2S3. The function of EIF2S3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1254. Eukaryotic Translation Initiation Factor 4 Gamma, 2 (EIF4G2, Accession NM\_001418) is another VGAM1929 host target gene. EIF4G2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF4G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4G2 BINDING SITE, designated SEQ ID:7118, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64669] Another function of VGAM1929 is therefore inhibition of Eukaryotic Translation Initiation Factor 4 Gamma, 2 (EIF4G2, Accession NM\_001418), a gene which is a repressor of translation. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF4G2. The function of EIF4G2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1065. Eukaryotic Translation Initiation Factor 5A2 (EIF5A2, Accession NM\_020390) is another VGAM1929 host target gene. EIF5A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF5A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF5A2 BINDING SITE, designated SEQ ID:21662, to the nucleotide sequence of



VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64670] Another function of VGAM1929 is therefore inhibition of Eukaryotic Translation Initiation Factor 5A2 (EIF5A2, Accession NM\_020390). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF5A2. Engulfment and Cell Motility 1 (ced-12 homolog, *C. elegans*) (ELMO1, Accession NM\_130442) is another VGAM1929 host target gene. ELMO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELMO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELMO1 BINDING SITE, designated SEQ ID:28202, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64671] Another function of VGAM1929 is therefore inhibition of Engulfment and Cell Motility 1 (ced-12 homolog, *C. elegans*) (ELMO1, Accession NM\_130442). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with ELMO1. Enamelin (ENAM, Accession NM\_031889) is another VGAM1929 host target gene. ENAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENAM BINDING SITE, designated SEQ ID:25635, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64672] Another function of VGAM1929 is therefore inhibition of Enamelin (ENAM, Accession NM\_031889). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENAM. EphA3 (EPHA3, Accession NM\_005233) is another VGAM1929 host target gene. EPHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA3 BINDING SITE, designated SEQ ID:11742, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA,

also designated SEQ ID:4640.

[64673] Another function of VGAM1929 is therefore inhibition of EphA3 (EPHA3, Accession NM\_005233), a gene which binds to ephrin-a2, -a3, -a4 and -a5. could play a role in lymphoid function. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA3. The function of EPHA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM164.ErbB2 Interacting Protein (ERBB2IP, Accession NM\_018695) is another VGAM1929 host target gene. ERBB2IP BINDING SITE1 and ERBB2IP BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ERBB2IP, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERBB2IP BINDING SITE1 and ERBB2IP BINDING SITE2, designated SEQ ID:20770 and SEQ ID:20773 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64674] Another function of VGAM1929 is therefore inhibition of

ErbB2 Interacting Protein (ERBB2IP, Accession NM\_018695), a gene which ERBB2 interacting protein; acts as an adaptor for the receptor ERBB2/HER2. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERBB2IP. The function of ERBB2IP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1019. Fatty-acid-Coenzyme A Ligase, Long-chain 4 (FACL4, Accession NM\_004458) is another VGAM1929 host target gene. FACL4 BINDING SITE1 and FACL4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FACL4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FACL4 BINDING SITE1 and FACL4 BINDING SITE2, designated SEQ ID:10763 and SEQ ID:23253 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64675] Another function of VGAM1929 is therefore inhibition of Fatty-acid-Coenzyme A Ligase, Long-chain 4 (FACL4, Ac-

cession NM\_004458). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FACL4. Flap Structure-specific Endonuclease 1 (FEN1, Accession NM\_004111) is another VGAM1929 host target gene. FEN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FEN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FEN1 BINDING SITE, designated SEQ ID:10322, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64676] Another function of VGAM1929 is therefore inhibition of Flap Structure-specific Endonuclease 1 (FEN1, Accession NM\_004111), a gene which Flap endonuclease; double-stranded DNA 5'-3' exonuclease. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FEN1. The function of FEN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1217. Fibronectin Leucine Rich Transmembrane

Protein 2 (FLRT2, Accession NM\_013231) is another VGAM1929 host target gene. FLRT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14889, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64677] Another function of VGAM1929 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM\_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Forkhead Box F1 (FOXF1, Accession NM\_001451) is another VGAM1929 host target gene. FOXF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FOXF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXF1 BINDING SITE, designated SEQ ID:7184, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64678] Another function of VGAM1929 is therefore inhibition of Forkhead Box F1 (FOXF1, Accession NM\_001451), a gene which is a probable transcription activator for a number of lung-specific genes. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXF1. The function of FOXF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM292.FREB (Accession NM\_032738) is another VGAM1929 host target gene. FREB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FREB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FREB BINDING SITE, design-

nated SEQ ID:26468, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64679] Another function of VGAM1929 is therefore inhibition of FREB (Accession NM\_032738). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FREB. FXYP Domain Containing Ion Transport Regulator 6 (FXYP6, Accession NM\_022003) is another VGAM1929 host target gene. FXYP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FXYP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FXYP6 BINDING SITE, designated SEQ ID:22549, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64680] Another function of VGAM1929 is therefore inhibition of FXYP Domain Containing Ion Transport Regulator 6 (FXYP6, Accession NM\_022003). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FXYP6.



GTP Cyclohydrolase 1 (dopa-responsive dystonia) (GCH1, Accession NM\_000161) is another VGAM1929 host target gene. GCH1 BINDING SITE1 and GCH1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GCH1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCH1 BINDING SITE1 and GCH1 BINDING SITE2, designated SEQ ID:5666 and SEQ ID:5667 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64681] Another function of VGAM1929 is therefore inhibition of GTP Cyclohydrolase 1 (dopa-responsive dystonia) (GCH1, Accession NM\_000161). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCH1. Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM\_000838) is another VGAM1929 host target gene. GRM1 BINDING SITE1 and GRM1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GRM1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM1 BINDING SITE1 and GRM1 BINDING SITE2, designated SEQ ID:6500 and SEQ ID:6501 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64682] Another function of VGAM1929 is therefore inhibition of Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM\_000838), a gene which promotes phosphoinositide hydrolysis. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM1. The function of GRM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM786. Histone Deacetylase 4 (HDAC4, Accession NM\_006037) is another VGAM1929 host target gene. HDAC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HDAC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC4 BINDING SITE, designated SEQ ID:12662, to the nucleotide se-

quence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64683] Another function of VGAM1929 is therefore inhibition of Histone Deacetylase 4 (HDAC4, Accession NM\_006037), a gene which is responsible for the deacetylation of lysine residues on the n-terminal part of the core histones and may mediate transcriptional regulation. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC4. The function of HDAC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM264. Hepatoma-derived Growth Factor (high-mobility group protein 1-like) (HDGF, Accession NM\_004494) is another VGAM1929 host target gene. HDGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HDGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDGF BINDING SITE, designated SEQ ID:10833, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64684] Another function of VGAM1929 is therefore inhibition of Hepatoma-derived Growth Factor (high-mobility group protein 1-like) (HDGF, Accession NM\_004494), a gene which is a heparin-binding protein, with mitogenic activity for fibroblasts. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDGF. The function of HDGF has been established by previous studies. Nakamura et al. (1994) purified a novel hepatoma-derived growth factor from the conditioned medium of human hepatoma-derived cell line HuH-7. Molecular cloning of a cDNA from the cDNA library of the same cell line was done on the basis of the N-terminal amino acid sequence. The cDNA was 2.4 kb long and the deduced amino acid sequence contained 240 amino acids without a signal peptide-like N-terminal hydrophobic sequence. The primary sequence shared homology with the high mobility group-1 protein (OMIM Ref. No. 163905); they showed 23.4% amino acid identity and 35.6% amino acid similarity. Immunofluorescence study showed that HDGF is localized in the cytoplasm of hepatoma cells and northern blots showed that it is expressed ubiquitously in normal tissues and tumor cell lines. Nakamura et al. (1994) suggested

that it is a novel heparin-binding protein with mitogenic activity for fibroblasts. HDGF is ubiquitously expressed in normal tissues and tumor cell lines. By PCR screening of a commercial monochromosomal hybrid panel, Wanschura et al. (1996) mapped HDGF to the X chromosome. By fluorescence in situ hybridization, they determined the sub-chromosomal localization to be Xq25. Whereas a major group of the HMG protein family has been mapped to chromosomal segments frequently involved in the tumorigenesis of benign solid tumors, no tumor association for the Xq25 region was known.

[64685] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64686] Nakamura, H.; Izumoto, Y.; Kambe, H.; Kuroda, T.; Mori, T.; Kawamura, K.; Yamamoto, H.; Kishimoto, T. : Molecular cloning of complementary DNA for a novel human hepatoma-derived growth factor: its homology with high mobility group-1 protein. J. Biol. Chem. 269: 25143-25149, 1994. ; and

[64687] Wanschura, S.; Schoenmakers, E. F. P. M.; Huysmans, C.; Bartnitzke, S.; Van de Ven, W. J. M.; Bullerdiek, J. : Mapping of the gene encoding the human hepatoma-derived

growth factor (HDG.

[64688] Further studies establishing the function and utilities of HDGF are found in John Hopkins OMIM database record ID 300043, and in cited publications numbered 8839–8840 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542) is another VGAM1929 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45222, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64689] Another function of VGAM1929 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. Hypermethylated In Cancer 1 (HIC1, Accession XM\_113307) is another VGAM1929 host target gene. HIC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HIC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC1 BINDING SITE, designated SEQ ID:42210, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64690] Another function of VGAM1929 is therefore inhibition of Hypermethylated In Cancer 1 (HIC1, Accession XM\_113307), a gene which is a transcriptional repressor and may act as a tumor suppressor. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC1. The function of HIC1 has been established by previous studies. The human HIC1 (hypermethylated in cancer) gene maps to 17p13.3 and is deleted in the contiguous

gene disorder Miller–Dieker syndrome (MDS; 247200) (Makos Wales et al., 1995; Chong et al., 1996). Grimm et al. (1999) isolated the murine Hic1 gene, which encodes a zinc finger protein with a poxvirus and zinc finger (POZ) domain. Comparison of genomic and cDNA sequences predicted 2 exons for the murine Hic1 gene. The second exon exhibits 88% identity at the DNA level to the corresponding region of the human HIC1 gene. During embryonic development, Hic1 is expressed in mesenchymes of the sclerotomes, lateral body wall, limb, and craniofacial regions embedding the outgrowing peripheral nerves during their differentiation. During fetal development, Hic1 is also expressed in mesenchymes apposed to the precartilaginous condensations, at many interfaces to budding epithelia of inner organs, and weakly in muscles. Grimm et al. (1999) observed activation of Hic1 expression in the embryonic anlagen of many tissues displaying anomalies in MDS patients. Besides lissencephaly, MDS patients exhibit facial dysmorphism and frequently additional birth defects, e.g., anomalies of the heart, kidney, gastrointestinal tract, and the limbs. Thus, HIC1 activity may correlate with the defective development of the nose, jaws, extremities, gastrointestinal tract, and kidney in MDS pa-



tients. Animal model experiments lend further support to the function of HIC1. The location of HIC1 in the Miller–Dieker syndrome critical deletion region on 17p13.3 makes it a candidate gene for involvement in the MDS gene deletion syndrome. To study the function of murine Hic1 in development, Carter et al. (2000) created Hic1–deficient mice. They found that these animals died perinatally and exhibited varying combinations of gross developmental defects throughout the second half of development, including acrania, exencephaly, cleft palate, limb anomalies, and omphalocele. These abnormalities demonstrated a role for Hic1 in the development of structures affected in the Miller–Dieker syndrome, and provided functional evidence to strengthen its candidacy as a gene involved in that disorder.

[64691] It is appreciated that the abovementioned animal model for HIC1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[64692] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64693] Carter, M. G.; Johns, M. A.; Zeng, X.; Zhou, L.; Zink, M. C.;

Mankowski, J. L.; Donovan, D. M.; Baylin, S. B. : Mice deficient in the candidate tumor suppressor gene Hic1 exhibit developmental defects of structures affected in the Miller-Dieker syndrome. Hum. Molec. Genet. 9: 413-419, 2000. ; and

[64694] Grimm, C.; Sporle, R.; Schmid, T. E.; Adler, I.-D.; Adamski, J.; Schughart, K.; Graw, J. : Isolation and embryonic expression of the novel mouse gene Hic1, the homologue of HIC1, a cand.

[64695] Further studies establishing the function and utilities of HIC1 are found in John Hopkins OMIM database record ID 603825, and in cited publications numbered 5183-5186 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Homeo Box B5 (HOXB5, Accession NM\_002147) is another VGAM1929 host target gene. HOXB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXB5 BINDING SITE, designated SEQ ID:7925, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4640.

[64696] Another function of VGAM1929 is therefore inhibition of Homeo Box B5 (HOXB5, Accession NM\_002147), a gene which may regulate gene expression, morphogenesis and differentiation. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXB5. The function of HOXB5 has been established by previous studies. As reviewed by Acampora et al. (1989), the homeo box region 2 contains 9 homeo box genes in 180 kb of DNA on chromosome 17. The order, from 5-prime to 3-prime, is HOXB9 (HOX2E), HOXB8 (HOX2D), HOXB7 (HOX2C), HOXB6 (HOX2B), HOXB5 (HOX2A), HOXB4 (HOX2F), HOXB3 (HOX2G), HOXB2 (HOX2H), HOXB1 (HOX2I). Classical models of craniofacial development argue that the neural crest is prepatterned or preprogrammed to make specific head structures before its migration from the neural tube. In contrast, recent studies in several vertebrates, including mouse, chick, and zebrafish, have provided evidence for plasticity in patterning neural crest populations. Using tissue transposition and molecular analyses in avian embryos, Trainor et al. (2002) reconciled these findings by demonstrating that classical manipulation experiments,

which form the basis of the pre patterning model, involved transplantation of a local signaling center, the isthmic organizer. FGF8 (OMIM Ref. No. 600483) signaling from the isthmus alters HOXA2 expression and consequently branchial arch patterning, demonstrating that neural crest cells are patterned by environmental signals.

[64697] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64698] Acampora, D.; D'Esposito, M.; Faiella, A.; Pannese, M.; Migliaccio, E.; Morelli, F.; Stornaiuolo, A.; Nigro, V.; Simone, A.; Boncinelli, E. : The human HOX gene family. Nucleic Acids Res. 17: 10385–10402, 1989. ; and

[64699] Trainor, P. A.; Ariza-McNaughton, L.; Krumlauf, R. : Role of the isthmus and FGFs in resolving the paradox of neural crest plasticity and pre patterning. Science 295: 1288–1291, 2002.

[64700] Further studies establishing the function and utilities of HOXB5 are found in John Hopkins OMIM database record ID 142960, and in cited publications numbered 5207–2646, 5213–2651, 5217–5218, 2652–265 and 11977 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Homeo

Box C4 (HOXC4, Accession NM\_014620) is another VGAM1929 host target gene. HOXC4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HOXC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXC4 BINDING SITE, designated SEQ ID:15974, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64701] Another function of VGAM1929 is therefore inhibition of Homeo Box C4 (HOXC4, Accession NM\_014620), a gene which is part of a developmental regulatory system that provides cells with specific positional identities on the anterior-posterior axis. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXC4. The function of HOXC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Heat Shock 70kDa Protein 4 (HSPA4, Accession XM\_114482) is another VGAM1929 host target gene. HSPA4 BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by HSPA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPA4 BINDING SITE, designated SEQ ID:42976, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64702] Another function of VGAM1929 is therefore inhibition of Heat Shock 70kDa Protein 4 (HSPA4, Accession XM\_114482). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPA4. Isoprenylcysteine Carboxyl Methyltransferase (ICMT, Accession NM\_012405) is another VGAM1929 host target gene. ICMT BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ICMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICMT BINDING SITE, designated SEQ ID:14782, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64703] Another function of VGAM1929 is therefore inhibition of Isoprenylcysteine Carboxyl Methyltransferase (ICMT, Accession NM\_012405). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICMT. Interleukin 2 Receptor, Beta (IL2RB, Accession NM\_000878) is another VGAM1929 host target gene. IL2RB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL2RB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL2RB BINDING SITE, designated SEQ ID:6576, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64704] Another function of VGAM1929 is therefore inhibition of Interleukin 2 Receptor, Beta (IL2RB, Accession NM\_000878), a gene which is involved in receptor mediated endocytosis and transduces the mitogenic signals of il-2. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL2RB. The function of IL2RB and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM450. Integrin, Alpha 6 (ITGA6, Accession NM\_000210) is another VGAM1929 host target gene. ITGA6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ITGA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA6 BINDING SITE, designated SEQ ID:5706, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64705] Another function of VGAM1929 is therefore inhibition of Integrin, Alpha 6 (ITGA6, Accession NM\_000210). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA6. Jagged 2 (JAG2, Accession NM\_002226) is another VGAM1929 host target gene. JAG2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by JAG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAG2



BINDING SITE, designated SEQ ID:8007, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64706] Another function of VGAM1929 is therefore inhibition of Jagged 2 (JAG2, Accession NM\_002226), a gene which is a putative notch ligand involved in the mediation of notch signaling. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAG2. The function of JAG2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM136. Kinesin Family Member 1B (KIF1B, Accession NM\_015074) is another VGAM1929 host target gene. KIF1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF1B BINDING SITE, designated SEQ ID:17448, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64707] Another function of VGAM1929 is therefore inhibition of

Kinesin Family Member 1B (KIF1B, Accession NM\_015074), a gene which motor for anterograde transport of mitochondria. has a microtubule plus end-directed motility. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF1B. The function of KIF1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1026. Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession NM\_002293) is another VGAM1929 host target gene. LAMC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAMC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMC1 BINDING SITE, designated SEQ ID:8075, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64708] Another function of VGAM1929 is therefore inhibition of Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession NM\_002293), a gene which may mediate the attachment,

migration, and organization of cells into tissues. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAMC1. The function of LAMC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM812. LIM Domain Binding 3 (LDB3, Accession XM\_084376) is another VGAM1929 host target gene. LDB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LDB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDB3 BINDING SITE, designated SEQ ID:37562, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64709] Another function of VGAM1929 is therefore inhibition of LIM Domain Binding 3 (LDB3, Accession XM\_084376), a gene which could play a role during mating. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDB3. The function of LDB3 has been established by

previous studies. PDZ domain-containing proteins interact with each other in cytoskeletal assembly or with other proteins involved in targeting and clustering of membrane proteins. By screening a muscle cDNA library using a muscle EST sequence as the probe, Faulkner et al. (1999) obtained cDNAs encoding mouse and human ZASP. The deduced 283-amino acid human ZASP protein has an 85-residue N-terminal PDZ domain and shares significant similarity with the 734-amino acid protein encoded by the KIAA0613 cDNA isolated by Ishikawa et al. (1998).

Database, PCR, and genomic DNA analyses indicated the presence of alternatively spliced isoforms of ZASP that encode proteins of 470, 617, and 727 (KIAA0613) amino acids. Northern blot analysis detected a major 1.9-kb ZASP transcript that was most abundant in skeletal muscle and heart but absent in other tissues tested. Additional transcripts of 4.0 and 5.4 kb were detected when using a 5-prime rather than a 3-prime probe. RT-PCR analysis detected wide expression of KIAA0613, with weak or undetectable expression in liver, pancreas, and spleen (Ishikawa et al., 1998). Western blot analysis showed expression of 32- and 78-kD proteins in heart and muscle. Immunofluorescence microscopy demonstrated that ZASP

is expressed in pseudopodia and in the cytoplasm around the nucleus, and that it colocalizes with actin in the I-band. Immunoelectron microscopy localized ZASP within the Z-band. Yeast 2-hybrid analysis determined that the PDZ domain of ZASP interacts with the C terminus of alpha-actinin-2 (ACTN2; 102573

[64710] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64711] Faulkner, G.; Pallavicini, A.; Formentin, E.; Comelli, A.; Ievolella, C.; Trevisan, S.; Bortoletto, G.; Scannapieco, P.; Salamon, M.; Mouly, V.; Valle, G.; Lanfranchi, G. : ZASP: a new Z-band alternatively spliced PDZ-motif protein. J. Cell Biol. 146: 465-475, 1999. ; and

[64712] Ishikawa, K.; Nagase, T.; Suyama, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. X. The complete sequence.

[64713] Further studies establishing the function and utilities of LDB3 are found in John Hopkins OMIM database record ID 605906, and in cited publications numbered 74 and 9440 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LENG4 (Accession

NM\_024298) is another VGAM1929 host target gene.

LENG4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LENG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LENG4 BINDING SITE, designated SEQ ID:23587, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64714] Another function of VGAM1929 is therefore inhibition of LENG4 (Accession NM\_024298), a gene which may be a transmembrane protein. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LENG4. The function of LENG4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259. Leukemia Inhibitory Factor Receptor (LIFR, Accession NM\_002310) is another VGAM1929 host target gene. LIFR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LIFR, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIFR BINDING SITE, designated SEQ ID:8101, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64715] Another function of VGAM1929 is therefore inhibition of Leukemia Inhibitory Factor Receptor (LIFR, Accession NM\_002310). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIFR. Low Density Lipoprotein Receptor-related Protein 8, Apolipoprotein E Receptor (LRP8, Accession NM\_033300) is another VGAM1929 host target gene. LRP8 BINDING SITE1 and LRP8 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LRP8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP8 BINDING SITE1 and LRP8 BINDING SITE2, designated SEQ ID:27129 and SEQ ID:11005 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64716] Another function of VGAM1929 is therefore inhibition of

Low Density Lipoprotein Receptor-related Protein 8, Apolipoprotein E Receptor (LRP8, Accession NM\_033300), a gene which binds vldl and transports it into cells by endocytosis. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP8. The function of LRP8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Leucine Zipper, Putative Tumor Suppressor 1 (LZTS1, Accession NM\_021020) is another VGAM1929 host target gene. LZTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LZTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTS1 BINDING SITE, designated SEQ ID:22010, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64717] Another function of VGAM1929 is therefore inhibition of Leucine Zipper, Putative Tumor Suppressor 1 (LZTS1, Accession NM\_021020), a gene which Zygin 1; may have a



role in axonal outgrowth; has similarity to *C. elegans* UNC-76. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTS1. The function of LZTS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM890.

MAP-kinase Activating Death Domain (MADD, Accession NM\_130470) is another VGAM1929 host target gene. MADD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MADD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADD BINDING SITE, designated SEQ ID:28238, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64718] Another function of VGAM1929 is therefore inhibition of MAP-kinase Activating Death Domain (MADD, Accession NM\_130470), a gene which may regulate two different pathways for neural activities. interacts with the type-1 tumor necrosis factor receptor (TNFR1); death domain-

containing protein. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADD. The function of MADD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430.MAD, Mothers Against Decapentaplegic Homolog 4 (Drosophila) (MADH4, Accession NM\_005359) is another VGAM1929 host target gene. MADH4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MADH4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADH4 BINDING SITE, designated SEQ ID:11833, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64719] Another function of VGAM1929 is therefore inhibition of MAD, Mothers Against Decapentaplegic Homolog 4 (Drosophila) (MADH4, Accession NM\_005359), a gene which common mediator of signal transduction by  $\text{tgf-}\beta$  (transforming growth factor) superfamily; *smad4* is the common *smad* (co-*smad*). promotes binding of the

smad2/sm44/fast-1 complex to dna and provides an activation function required for smad1 or smad2 to stimulate transcription. may act as a tumor suppressor. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADH4. The function of MADH4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. Monoamine Oxidase B (MAOB, Accession XM\_010261) is another VGAM1929 host target gene. MAOB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAOB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAOB BINDING SITE, designated SEQ ID:30149, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64720] Another function of VGAM1929 is therefore inhibition of Monoamine Oxidase B (MAOB, Accession XM\_010261). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with MAOB. Mannose-binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM\_000242) is another VGAM1929 host target gene. MBL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBL2 BINDING SITE, designated SEQ ID:5762, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64721] Another function of VGAM1929 is therefore inhibition of Mannose-binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM\_000242). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBL2. Muscleblind-like (Drosophila) (MBNL, Accession NM\_021038) is another VGAM1929 host target gene. MBNL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MBNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of MBNL BINDING SITE, designated SEQ ID:22027, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64722] Another function of VGAM1929 is therefore inhibition of Muscleblind-like (Drosophila) (MBNL, Accession NM\_021038), a gene which binds to cug triplet repeat expansion dsrna (by similarity). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBNL. The function of MBNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. MADS Box Transcription Enhancer Factor 2, Polypeptide C (myocyte enhancer factor 2C) (MEF2C, Accession NM\_002397) is another VGAM1929 host target gene. MEF2C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEF2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEF2C BINDING SITE, designated SEQ ID:8213, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ

ID:4640.

[64723] Another function of VGAM1929 is therefore inhibition of MADS Box Transcription Enhancer Factor 2, Polypeptide C (myocyte enhancer factor 2C) (MEF2C, Accession NM\_002397), a gene which regulates muscle-specific and mitogen-inducible genes. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEF2C. The function of MEF2C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM386.Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog (mouse) (MEIS1, Accession NM\_002398) is another VGAM1929 host target gene. MEIS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEIS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEIS1 BINDING SITE, designated SEQ ID:8220, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64724] Another function of VGAM1929 is therefore inhibition of

Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog (mouse) (MEIS1, Accession NM\_002398), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEIS1. The function of MEIS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

#### VGAM894.Meningioma Expressed Antigen 5

(hyaluronidase) (MGEA5, Accession NM\_012215) is another VGAM1929 host target gene. MGEA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGEA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGEA5 BINDING SITE, designated SEQ ID:14521, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64725] Another function of VGAM1929 is therefore inhibition of Meningioma Expressed Antigen 5 (hyaluronidase) (MGEA5, Accession NM\_012215), a gene which has a hyaluronidase

activity. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGEA5. The function of MGEA5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM801. Midline 1 (Opitz/BBB syndrome) (MID1, Accession NM\_000381) is another VGAM1929 host target gene. MID1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MID1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MID1 BINDING SITE, designated SEQ ID:5957, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64726] Another function of VGAM1929 is therefore inhibition of Midline 1 (Opitz/BBB syndrome) (MID1, Accession NM\_000381). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MID1. Myeloid Leukemia Factor 2 (MLF2, Accession NM\_005439) is another VGAM1929 host target gene. MLF2 BINDING SITE is HOST



TARGET binding site found in the 3` untranslated region of mRNA encoded by MLF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLF2 BINDING SITE, designated SEQ ID:11925, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64727] Another function of VGAM1929 is therefore inhibition of Myeloid Leukemia Factor 2 (MLF2, Accession NM\_005439). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLF2. Matrix Metalloproteinase 19 (MMP19, Accession NM\_022790) is another VGAM1929 host target gene. MMP19 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MMP19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP19 BINDING SITE, designated SEQ ID:23075, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64728] Another function of VGAM1929 is therefore inhibition of Matrix Metalloproteinase 19 (MMP19, Accession NM\_022790). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP19. MAX Binding Protein (MNT, Accession NM\_020310) is another VGAM1929 host target gene. MNT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MNT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MNT BINDING SITE, designated SEQ ID:21562, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64729] Another function of VGAM1929 is therefore inhibition of MAX Binding Protein (MNT, Accession NM\_020310). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MNT. Antigen Identified By Monoclonal Antibody MRC OX-2 (MOX2, Accession XM\_039962) is another VGAM1929 host target gene. MOX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by MOX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOX2 BINDING SITE, designated SEQ ID:33237, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64730] Another function of VGAM1929 is therefore inhibition of Antigen Identified By Monoclonal Antibody MRC OX-2 (MOX2, Accession XM\_039962). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOX2. Membrane-spanning 4-domains, Subfamily A, Member 1 (MS4A1, Accession NM\_000139) is another VGAM1929 host target gene. MS4A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MS4A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MS4A1 BINDING SITE, designated SEQ ID:5632, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64731] Another function of VGAM1929 is therefore inhibition of Membrane-spanning 4-domains, Subfamily A, Member 1 (MS4A1, Accession NM\_000139), a gene which may be involved in the regulation of b-cell activation and proliferation. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MS4A1. The function of MS4A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM362. Myotubularin Related Protein 3 (MTMR3, Accession NM\_021090) is another VGAM1929 host target gene. MTMR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTMR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR3 BINDING SITE, designated SEQ ID:22071, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64732] Another function of VGAM1929 is therefore inhibition of Myotubularin Related Protein 3 (MTMR3, Accession

NM\_021090), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTMR3. The function of MTMR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1718.

MAX Interacting Protein 1 (MXI1, Accession NM\_130439) is another VGAM1929 host target gene. MXI1 BINDING SITE1 and MXI1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MXI1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MXI1 BINDING SITE1 and MXI1 BINDING SITE2, designated SEQ ID:28194 and SEQ ID:12584 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64733] Another function of VGAM1929 is therefore inhibition of MAX Interacting Protein 1 (MXI1, Accession NM\_130439), a gene which acts as a tumor suppressor in vivo, engages the MYC network in a functionally relevant manner. Ac-

cordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MXI1. The function of MXI1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM128. NCK-associated Protein 1 (NCKAP1, Accession NM\_013436) is another VGAM1929 host target gene. NCKAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCKAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCKAP1 BINDING SITE, designated SEQ ID:15096, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64734] Another function of VGAM1929 is therefore inhibition of NCK-associated Protein 1 (NCKAP1, Accession NM\_013436). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCKAP1. Nuclear Receptor Coactivator 3 (NCOA3, Accession NM\_006534) is another VGAM1929 host target gene. NCOA3 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NCOA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCOA3 BINDING SITE, designated SEQ ID:13288, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64735] Another function of VGAM1929 is therefore inhibition of Nuclear Receptor Coactivator 3 (NCOA3, Accession NM\_006534), a gene which directly binds nuclear receptors and stimulates the transcriptional activities in hormone-dependent fashion. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCOA3. The function of NCOA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM215. Nebulin (NEB, Accession NM\_004543) is another VGAM1929 host target gene. NEB BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NEB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEB BINDING SITE, designated SEQ ID:10892, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64736] Another function of VGAM1929 is therefore inhibition of Nebulin (NEB, Accession NM\_004543). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEB. NIMA (never in mitosis gene a)-related Kinase 4 (NEK4, Accession NM\_003157) is another VGAM1929 host target gene. NEK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEK4 BINDING SITE, designated SEQ ID:9138, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64737] Another function of VGAM1929 is therefore inhibition of NIMA (never in mitosis gene a)-related Kinase 4 (NEK4, Accession NM\_003157). Accordingly, utilities of



VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEK4. Nuclear Factor (erythroid-derived 2)-like 1 (NFE2L1, Accession NM\_003204) is another VGAM1929 host target gene. NFE2L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFE2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFE2L1 BINDING SITE, designated SEQ ID:9199, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64738] Another function of VGAM1929 is therefore inhibition of Nuclear Factor (erythroid-derived 2)-like 1 (NFE2L1, Accession NM\_003204), a gene which may regulate expression of ferritin genes. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFE2L1. The function of NFE2L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM369.Nerve Growth Factor Receptor (TNFRSF16) As-

sociated Protein 1 (NGFRAP1, Accession NM\_014380) is another VGAM1929 host target gene. NGFRAP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NGFRAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGFRAP1 BINDING SITE, designated SEQ ID:15715, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64739] Another function of VGAM1929 is therefore inhibition of Nerve Growth Factor Receptor (TNFRSF16) Associated Protein 1 (NGFRAP1, Accession NM\_014380), a gene which may play an important role in the pathogenesis of neuro-genetic diseases. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGFRAP1. The function of NGFRAP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM260.Nipsnap Homolog 1 (C. elegans) (NIPSNAP1, Accession NM\_003634) is another VGAM1929 host target gene. NIPSNAP1 BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by NIPSNAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIPSNAP1 BINDING SITE, designated SEQ ID:9701, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64740] Another function of VGAM1929 is therefore inhibition of Nipsnap Homolog 1 (*C. elegans*) (NIPSNAP1, Accession NM\_003634). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIPSNAP1. Neuronal Cell Adhesion Molecule (NRCAM, Accession NM\_005010) is another VGAM1929 host target gene. NRCAM BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NRCAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRCAM BINDING SITE, designated SEQ ID:11450, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64741] Another function of VGAM1929 is therefore inhibition of Neuronal Cell Adhesion Molecule (NRCAM, Accession NM\_005010), a gene which functions as a cell surface protein and belongs to the immunoglobulin superfamily. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRCAM. The function of NRCAM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM268.2'-5'-oligoadenylate Synthetase 2, 69/71kDa (OAS2, Accession NM\_016817) is another VGAM1929 host target gene. OAS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAS2 BINDING SITE, designated SEQ ID:18806, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64742] Another function of VGAM1929 is therefore inhibition of 2'-5'-oligoadenylate Synthetase 2, 69/71kDa (OAS2, Ac-

cession NM\_016817), a gene which may play a role in mediating resistance to virus infection, control of cell growth, differentiation, and apoptosis. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAS2. The function of OAS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1498. Optic Atrophy 1 (autosomal dominant) (OPA1, Accession NM\_130833) is another VGAM1929 host target gene. OPA1 BINDING SITE1 through OPA1 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OPA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPA1 BINDING SITE1 through OPA1 BINDING SITE5, designated SEQ ID:28322, SEQ ID:28330, SEQ ID:28338, SEQ ID:28346 and SEQ ID:28354 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64743] Another function of VGAM1929 is therefore inhibition of Optic Atrophy 1 (autosomal dominant) (OPA1, Accession

NM\_130833). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPA1. Purinergic Receptor P2Y, G-protein Coupled, 1 (P2RY1, Accession NM\_002563) is another VGAM1929 host target gene. P2RY1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P2RY1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RY1 BINDING SITE, designated SEQ ID:8411, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64744] Another function of VGAM1929 is therefore inhibition of Purinergic Receptor P2Y, G-protein Coupled, 1 (P2RY1, Accession NM\_002563), a gene which plays an essential role in thrombotic states. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RY1. The function of P2RY1 has been established by previous studies. P2 purinoceptors have been broadly classified as P2X receptors (e.g., 600843), which are ATP-gated channels; P2Z receptors, which mediate nonselective pores in

mast cells; and P2Y receptors, a family of G protein-coupled receptors. Based on the recommendation for nomenclature of P2 purinoceptors, the P2Y purinoceptors were numbered in the order of cloning. Ayyanathan et al. (1996) noted that P2Y1, P2Y2 (PR2Y2; 600041), and P2Y3 have been cloned from a variety of species. P2Y1 responds to both ADP and ATP. The P2Y2 receptor cDNA was cloned in the human and this receptor was known as P2U under previous nomenclature. Ayyanathan et al. (1996) cloned the human P2Y1 receptor (P2RY1) and its 2 alternately polyadenylated forms of mRNA. The P2Y1 purinoceptor was also cloned from a human placenta cDNA library by Leon et al. (1996). They found that the gene encodes a 372-amino acid polypeptide. Northern blot analysis revealed 2 transcripts of 4.6 and 7.5 kb which were expressed in many tissues. Using oligonucleotide primers specific for the human P2Y1 purinergic receptor, Ayyanathan et al. (1996) amplified a region from genomic DNA from a panel of mouse/human somatic cell hybrid cell lines and localized the P2Y1 gene to human chromosome 3. By sequence tagged site (STS) mapping utilizing the National Center for Biotechnology Information (NCBI) database, Somers et al. (1997) mapped the

P2RY1 gene between flanking markers D3S1279 and D3S1280 at a position 173 to 174 cM from the most telomeric markers on the short arm of chromosome 3. Animal model experiments lend further support to the function of P2RY1. Leon et al. (1999) generated P2Y1-null mice to define the physiologic role of the P2Y1 receptor. These mice were viable with no apparent abnormalities affecting their development, survival, reproduction, or morphology of platelets, and the platelet count in these animals was identical to that of wildtype mice. However, platelets from P2Y1-deficient mice were unable to aggregate in response to usual concentrations of ADP and displayed impaired aggregation to other agonists, while high concentrations of ADP induced platelet aggregation without shape change. In addition, ADP-induced inhibition of adenylyl cyclase still occurred, demonstrating the existence of an ADP receptor distinct from P2Y1. P2Y1-null mice had no spontaneous bleeding tendency but were resistant to thromboembolism induced by intravenous injection of ADP or collagen and adrenaline. Hence, the P2Y1 receptor plays an essential role in thrombotic states and represents a potential target for antithrombotic drugs.



[64745] It is appreciated that the abovementioned animal model for P2RY1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[64746] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64747] Ayyanathan, K.; Webbs, T. E.; Sandhu, A. K.; Athwal, R. S.; Barnard, E. A.; Kunapuli, S. P. : Cloning and chromosomal localization of the human P2Y1 purinoceptor. Biochem. Biophys. Res. Commun. 218: 783–788, 1996. ; and

[64748] Leon, C.; Hechler, B.; Freund, M.; Eckly, A.; Vial, C.; Ohlmann, P.; Dierich, A.; LeMeur, M.; Cazenave, J.-P.; Gachet, C. : Defective platelet aggregation and increased resistance to thr.

[64749] Further studies establishing the function and utilities of P2RY1 are found in John Hopkins OMIM database record ID 601167, and in cited publications numbered 9467–947 and 7718 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphoribosylaminoimidazole Carboxylase, Phosphoribosylaminoimidazole Succinocarboxamide Synthetase (PAICS, Accession NM\_006452) is another

VGAM1929 host target gene. PAICS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PAICS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAICS BINDING SITE, designated SEQ ID:13165, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64750] Another function of VGAM1929 is therefore inhibition of Phosphoribosylaminoimidazole Carboxylase, Phosphoribosylaminoimidazole Succinocarboxamide Synthetase (PAICS, Accession NM\_006452), a gene which is required for purine biosynthesis. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAICS. The function of PAICS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM894. Phosphodiesterase 7A (PDE7A, Accession XM\_037534) is another VGAM1929 host target gene. PDE7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE7A,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE7A BINDING SITE, designated SEQ ID:32642, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64751] Another function of VGAM1929 is therefore inhibition of Phosphodiesterase 7A (PDE7A, Accession XM\_037534), a gene which is a CAMP-specific phosphodiesterase 7A and plays a role in signal transduction. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE7A. The function of PDE7A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1662. Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM\_003768) is another VGAM1929 host target gene. PEA15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEA15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PEA15 BINDING SITE, designated SEQ ID:9849, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64752] Another function of VGAM1929 is therefore inhibition of Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM\_003768), a gene which is a phosphoprotein and involved in glucose uptake. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEA15. The function of PEA15 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM949. Period Homolog 2 (Drosophila) (PER2, Accession NM\_022817) is another VGAM1929 host target gene. PER2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER2 BINDING SITE, designated SEQ ID:23094, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64753] Another function of VGAM1929 is therefore inhibition of Period Homolog 2 (Drosophila) (PER2, Accession NM\_022817), a gene which Period homolog 2; putative circadian clock protein; has a PAS dimerization domain. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER2. The function of PER2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM\_138694) is another VGAM1929 host target gene. PKHD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKHD1 BINDING SITE, designated SEQ ID:28939, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64754] Another function of VGAM1929 is therefore inhibition of Polycystic Kidney and Hepatic Disease 1 (autosomal recessive)

sive) (PKHD1, Accession NM\_138694). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKHD1. Pleiomorphic Adenoma Gene 1 (PLAG1, Accession NM\_002655) is another VGAM1929 host target gene. PLAG1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAG1 BINDING SITE, designated SEQ ID:8519, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64755] Another function of VGAM1929 is therefore inhibition of Pleiomorphic Adenoma Gene 1 (PLAG1, Accession NM\_002655), a gene which contains a zinc finger domain. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAG1. The function of PLAG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM29. Pleckstrin

(PLEK, Accession NM\_002664) is another VGAM1929 host target gene. PLEK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLEK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLEK BINDING SITE, designated SEQ ID:8532, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64756] Another function of VGAM1929 is therefore inhibition of Pleckstrin (PLEK, Accession NM\_002664), a gene which is the major protein kinase c substrate of platelets. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLEK. The function of PLEK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.POU Domain, Class 3, Transcription Factor 1 (POU3F1, Accession XM\_001334) is another VGAM1929 host target gene. POU3F1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU3F1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU3F1 BINDING SITE, designated SEQ ID:29833, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64757] Another function of VGAM1929 is therefore inhibition of POU Domain, Class 3, Transcription Factor 1 (POU3F1, Accession XM\_001334), a gene which involves in early embryogenesis and neurogenesis. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU3F1. The function of POU3F1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM85. Peroxisome Proliferative Activated Receptor, Gamma, Coactivator 1 (PPARGC1, Accession NM\_013261) is another VGAM1929 host target gene. PPARGC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPARGC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPARGC1 BINDING SITE, designated SEQ



ID:14933, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64758] Another function of VGAM1929 is therefore inhibition of Peroxisome Proliferative Activated Receptor, Gamma, Coactivator 1 (PPARGC1, Accession NM\_013261), a gene which may play a role in insulin sensitivity and thermogenesis. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPARGC1. The function of PPARGC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM952.PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM\_012231) is another VGAM1929 host target gene. PRDM2 BINDING SITE1 and PRDM2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PRDM2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM2 BINDING SITE1 and PRDM2 BINDING SITE2, designated SEQ ID:14535 and SEQ ID:18003 respectively, to the

nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64759] Another function of VGAM1929 is therefore inhibition of PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM\_012231), a gene which plays a role in transcriptional regulation during neuronal differentiation and pathogenesis of retinoblastoma. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM2. The function of PRDM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Protein Kinase, CAMP-dependent, Regulatory, Type I, Alpha (tissue specific extinguisher 1) (PRKAR1A, Accession NM\_002734) is another VGAM1929 host target gene. PRKAR1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKAR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAR1A BINDING SITE, designated SEQ ID:8608, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4640.

[64760] Another function of VGAM1929 is therefore inhibition of Protein Kinase, CAMP-dependent, Regulatory, Type I, Alpha (tissue specific extinguisher 1) (PRKAR1A, Accession NM\_002734). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAR1A. Proteasome (prosome, macropain) Subunit, Beta Type, 9 (large multifunctional protease 2) (PSMB9, Accession NM\_002800) is another VGAM1929 host target gene. PSMB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMB9 BINDING SITE, designated SEQ ID:8676, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64761] Another function of VGAM1929 is therefore inhibition of Proteasome (prosome, macropain) Subunit, Beta Type, 9 (large multifunctional protease 2) (PSMB9, Accession NM\_002800), a gene which is one component of a multicatalytic proteinase complex. Accordingly, utilities of

VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMB9. The function of PSMB9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1915. Pituitary Tumor-transforming 1 Interacting Protein (PTTG1IP, Accession NM\_004339) is another VGAM1929 host target gene. PTTG1IP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTTG1IP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTTG1IP BINDING SITE, designated SEQ ID:10534, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64762] Another function of VGAM1929 is therefore inhibition of Pituitary Tumor-transforming 1 Interacting Protein (PTTG1IP, Accession NM\_004339), a gene which facilitates the translocation of PTTG to the nucleus. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTTG1IP. The function of PTTG1IP and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM131. RAD51-like 1 (*S. cerevisiae*) (RAD51L1, Accession NM\_002877) is another VGAM1929 host target gene. RAD51L1 BINDING SITE1 and RAD51L1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD51L1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD51L1 BINDING SITE1 and RAD51L1 BINDING SITE2, designated SEQ ID:8788 and SEQ ID:28577 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64763] Another function of VGAM1929 is therefore inhibition of RAD51-like 1 (*S. cerevisiae*) (RAD51L1, Accession NM\_002877), a gene which is a member of the RAD51 family of strand-transfer proteins. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD51L1. The function of RAD51L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM1020.RAD51-like 3 (*S. cerevisiae*) (RAD51L3, Accession NM\_133630) is another VGAM1929 host target gene. RAD51L3 BINDING SITE1 through RAD51L3 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD51L3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD51L3 BINDING SITE1 through RAD51L3 BINDING SITE3, designated SEQ ID:28580, SEQ ID:8789 and SEQ ID:8809 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64764] Another function of VGAM1929 is therefore inhibition of RAD51-like 3 (*S. cerevisiae*) (RAD51L3, Accession NM\_133630), a gene which may have a role in dna repair and recombination. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD51L3. The function of RAD51L3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1310.Regulatory Factor X, 5 (influences HLA class

II expression) (RFX5, Accession NM\_000449) is another VGAM1929 host target gene. RFX5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RFX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX5 BINDING SITE, designated SEQ ID:6047, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64765] Another function of VGAM1929 is therefore inhibition of Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM\_000449), a gene which activates transcription from class ii mhc promoters. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFX5. The function of RFX5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Retinal G Protein Coupled Receptor (RGR, Accession NM\_002921) is another VGAM1929 host target gene. RGR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded

by RGR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGR BINDING SITE, designated SEQ ID:8825, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64766] Another function of VGAM1929 is therefore inhibition of Retinal G Protein Coupled Receptor (RGR, Accession NM\_002921), a gene which catalyse the isomerization of the chromophore by a retinochrome-like mechanism and act as a receptor for all-trans-and 11-cis-retinal. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGR. The function of RGR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1283. Ribonuclease, RNase A Family, K6 (RNASE6, Accession NM\_005615) is another VGAM1929 host target gene. RNASE6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RNASE6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-



plementarity of the nucleotide sequences of RNASE6 BINDING SITE, designated SEQ ID:12133, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64767] Another function of VGAM1929 is therefore inhibition of Ribonuclease, RNase A Family, K6 (RNASE6, Accession NM\_005615). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNASE6. Ring Finger Protein 4 (RNF4, Accession NM\_002938) is another VGAM1929 host target gene. RNF4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF4 BINDING SITE, designated SEQ ID:8842, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64768] Another function of VGAM1929 is therefore inhibition of Ring Finger Protein 4 (RNF4, Accession NM\_002938). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with RNF4. Ribosomal Protein L15 (RPL15, Accession NM\_002948) is another VGAM1929 host target gene. RPL15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPL15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPL15 BINDING SITE, designated SEQ ID:8861, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64769] Another function of VGAM1929 is therefore inhibition of Ribosomal Protein L15 (RPL15, Accession NM\_002948). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPL15. Ribonucleotide Reductase M2 B (TP53 inducible) (RRM2B, Accession XM\_042096) is another VGAM1929 host target gene. RRM2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RRM2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RRM2B BIND-

ING SITE, designated SEQ ID:33691, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64770] Another function of VGAM1929 is therefore inhibition of Ribonucleotide Reductase M2 B (TP53 inducible) (RRM2B, Accession XM\_042096). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RRM2B. Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754) is another VGAM1929 host target gene. RUNX1 BINDING SITE1 and RUNX1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RUNX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RUNX1 BINDING SITE1 and RUNX1 BINDING SITE2, designated SEQ ID:7499 and SEQ ID:7504 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64771] Another function of VGAM1929 is therefore inhibition of Runt-related Transcription Factor 1 (acute myeloid

leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RUNX1. Sodium Channel, Voltage-gated, Type III, Alpha Polypeptide (SCN3A, Accession NM\_006922) is another VGAM1929 host target gene. SCN3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCN3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN3A BINDING SITE, designated SEQ ID:13799, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64772] Another function of VGAM1929 is therefore inhibition of Sodium Channel, Voltage-gated, Type III, Alpha Polypeptide (SCN3A, Accession NM\_006922), a gene which may be important for maintaining neural membrane excitability. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN3A. The function of SCN3A and its association with various diseases and clinical condi-

tions, has been established by previous studies, as described hereinabove with reference to VGAM124. Sirtuin Silent Mating Type Information Regulation 2 Homolog 1 (*S. cerevisiae*) (SIRT1, Accession NM\_012238) is another VGAM1929 host target gene. SIRT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIRT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIRT1 BINDING SITE, designated SEQ ID:14544, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64773] Another function of VGAM1929 is therefore inhibition of Sirtuin Silent Mating Type Information Regulation 2 Homolog 1 (*S. cerevisiae*) (SIRT1, Accession NM\_012238), a gene which may function as intracellular regulatory protein with mono-ADP-ribosyltransferase activity. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIRT1. The function of SIRT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM244.Solute Carrier Family 20 (phosphate transporter), Member 2 (SLC20A2, Accession NM\_006749) is another VGAM1929 host target gene. SLC20A2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC20A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC20A2 BINDING SITE, designated SEQ ID:13601, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64774] Another function of VGAM1929 is therefore inhibition of Solute Carrier Family 20 (phosphate transporter), Member 2 (SLC20A2, Accession NM\_006749), a gene which is a sodium–phosphate symporter. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC20A2. The function of SLC20A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232.Solute Carrier Family 21 (organic anion transporter), Member 9 (SLC21A9, Acces–

sion NM\_007256) is another VGAM1929 host target gene. SLC21A9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC21A9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC21A9 BINDING SITE, designated SEQ ID:14128, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64775] Another function of VGAM1929 is therefore inhibition of Solute Carrier Family 21 (organic anion transporter), Member 9 (SLC21A9, Accession NM\_007256), a gene which is Moderately similar to SLC21A2 prostaglandin transporter. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC21A9. The function of SLC21A9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM894. Solute Carrier Family 2 (facilitated glucose transporter), Member 2 (SLC2A2, Accession NM\_000340) is another VGAM1929 host target gene. SLC2A2 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A2 BINDING SITE, designated SEQ ID:5892, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64776] Another function of VGAM1929 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter), Member 2 (SLC2A2, Accession NM\_000340). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A2. Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 7 (SLC4A7, Accession NM\_003615) is another VGAM1929 host target gene. SLC4A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC4A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A7 BINDING SITE, designated SEQ ID:9676, to the nucleotide sequence of VGAM1929 RNA,



herein designated VGAM RNA, also designated SEQ ID:4640.

[64777] Another function of VGAM1929 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 7 (SLC4A7, Accession NM\_003615), a gene which mediates the coupled movement of sodium and bicarbonate ions across the plasma membrane. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A7. The function of SLC4A7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM66. Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 8 (SLC4A8, Accession NM\_004858) is another VGAM1929 host target gene. SLC4A8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC4A8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A8 BINDING SITE, designated SEQ ID:11267, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4640.

[64778] Another function of VGAM1929 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 8 (SLC4A8, Accession NM\_004858), a gene which is a sodium bicarbonate cotransporter. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A8. The function of SLC4A8 has been established by previous studies. Sodium bicarbonate cotransporters (NBCs) mediate the coupled movement of sodium and bicarbonate ions across the plasma membrane. Soleimani and Burnham (2000) reviewed NBCs and their regulation in physiologic and pathophysiologic states. By screening human brain cDNAs for the potential to encode proteins that are at least 50 kD, Nagase et al. (1998) isolated a partial SLC4A8 cDNA, which they called KIAA0739, that lacks 5-prime coding sequence. The deduced 1,130-amino acid partial SLC4A8 protein shares 56.5% amino acid sequence identity with the human NBC1 (SLC4A4; 603345) variant kNBC across 953 residues. Analysis of SLC4A8 expression in 10 human tissues by RT-PCR followed by ELISA detected highest SLC4A8 expression in brain and testis, lower expression in pancreas,

kidney, lung, and ovary, and no expression in heart, liver, spleen, or skeletal muscle

[64779] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[64780] Soleimani, M.; Burnham, C. E. : Physiologic and molecular aspects of the Na(+):HCO(3-) cotransporter in health and disease processes. *Kidney Int.* 57: 371–384, 2000. ; and

[64781] Amlal, H.; Burnham, C. E.; Soleimani, M. : Characterization of Na(+)/HCO(3-) cotransporter isoform NBC-3. *Am. J. Physiol.* 276: F903–F913, 1999.

[64782] Further studies establishing the function and utilities of SLC4A8 are found in John Hopkins OMIM database record ID 605024, and in cited publications numbered 1083, 704 and 7959 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1 (SMARCD1, Accession NM\_139071) is another VGAM1929 host target gene. SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMARCD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2, designated SEQ ID:29143 and SEQ ID:9045 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64783] Another function of VGAM1929 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1 (SMARCD1, Accession NM\_139071), a gene which is involved in chromatin assembly and remodeling. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCD1. The function of SMARCD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152.SNL (Accession NM\_003088) is another VGAM1929 host target gene. SNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

SNL BINDING SITE, designated SEQ ID:9067, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64784] Another function of VGAM1929 is therefore inhibition of SNL (Accession NM\_003088), a gene which organizes filamentous actin into bundles with a minimum of 4.1:1 actin/fascin ratio. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNL. The function of SNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675. Sorting Nexin 9 (SNX9, Accession NM\_016224) is another VGAM1929 host target gene. SNX9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNX9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX9 BINDING SITE, designated SEQ ID:18330, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64785] Another function of VGAM1929 is therefore inhibition of

Sorting Nexin 9 (SNX9, Accession NM\_016224). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX9. Sorbin and SH3 Domain Containing 1 (SORBS1, Accession NM\_015385) is another VGAM1929 host target gene. SORBS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SORBS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORBS1 BINDING SITE, designated SEQ ID:17689, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64786] Another function of VGAM1929 is therefore inhibition of Sorbin and SH3 Domain Containing 1 (SORBS1, Accession NM\_015385), a gene which necessary for cell polarization during vegetative growth. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORBS1. The function of SORBS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM475.Spectrin, Beta, Non-erythrocytic 4 (SPTBN4, Accession NM\_025213) is another VGAM1929 host target gene. SPTBN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTBN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTBN4 BINDING SITE, designated SEQ ID:24884, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64787] Another function of VGAM1929 is therefore inhibition of Spectrin, Beta, Non-erythrocytic 4 (SPTBN4, Accession NM\_025213), a gene which is critical for the maintenance of plasma membrane shape and lipid asymmetry. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTBN4. The function of SPTBN4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM958.Sarcospan (Kras oncogene-associated gene) (SSPN, Accession NM\_005086) is another VGAM1929 host target gene. SSPN BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SSPN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSPN BINDING SITE, designated SEQ ID:11537, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64788] Another function of VGAM1929 is therefore inhibition of Sarcospan (Kras oncogene-associated gene) (SSPN, Accession NM\_005086), a gene which spans the muscle plasma membrane and forms a link between the f-actin cytoskeleton and the extracellular matrix. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSPN. The function of SSPN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM996. Staufen, RNA Binding Protein, Homolog 2 (Drosophila) (STAU2, Accession NM\_014393) is another VGAM1929 host target gene. STAU2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STAU2, corresponding to a



HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAU2 BINDING SITE, designated SEQ ID:15724, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64789] Another function of VGAM1929 is therefore inhibition of Staufen, RNA Binding Protein, Homolog 2 (Drosophila) (STAU2, Accession NM\_014393). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAU2. Transforming, Acidic Coiled-coil Containing Protein 1 (TACC1, Accession NM\_006283) is another VGAM1929 host target gene. TACC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TACC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TACC1 BINDING SITE, designated SEQ ID:12969, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64790] Another function of VGAM1929 is therefore inhibition of

Transforming, Acidic Coiled-coil Containing Protein 1 (TACC1, Accession NM\_006283). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TACC1. T-box, Brain, 1 (TBR1, Accession NM\_006593) is another VGAM1929 host target gene. TBR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBR1 BINDING SITE, designated SEQ ID:13358, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64791] Another function of VGAM1929 is therefore inhibition of T-box, Brain, 1 (TBR1, Accession NM\_006593), a gene which is of unknown function. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBR1. The function of TBR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM719. Transforming Growth Factor, Beta Receptor II

(70/80kDa) (TGFB2, Accession NM\_003242) is another VGAM1929 host target gene. TGFB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB2 BINDING SITE, designated SEQ ID:9242, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64792] Another function of VGAM1929 is therefore inhibition of Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM\_003242). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB2. Thrombomodulin (THBD, Accession NM\_000361) is another VGAM1929 host target gene. THBD BINDING SITE1 and THBD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by THBD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THBD BINDING SITE1 and THBD BINDING SITE2,

designated SEQ ID:5923 and SEQ ID:5924 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64793] Another function of VGAM1929 is therefore inhibition of Thrombomodulin (THBD, Accession NM\_000361). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THBD. TIA1 Cytotoxic Granule-associated RNA Binding Protein (TIA1, Accession NM\_022173) is another VGAM1929 host target gene. TIA1 BINDING SITE1 and TIA1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TIA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIA1 BINDING SITE1 and TIA1 BINDING SITE2, designated SEQ ID:22735 and SEQ ID:14838 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64794] Another function of VGAM1929 is therefore inhibition of TIA1 Cytotoxic Granule-associated RNA Binding Protein (TIA1, Accession NM\_022173), a gene which possesses nucleolytic activity against cytotoxic lymphocyte target

cells. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIA1. The function of TIA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM276. Tumor Necrosis Factor, Alpha-induced Protein 1 (endothelial) (TNFAIP1, Accession NM\_021137) is another VGAM1929 host target gene. TNFAIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFAIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFAIP1 BINDING SITE, designated SEQ ID:22112, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64795] Another function of VGAM1929 is therefore inhibition of Tumor Necrosis Factor, Alpha-induced Protein 1 (endothelial) (TNFAIP1, Accession NM\_021137). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFAIP1. TOX (Accession NM\_014729) is an-

other VGAM1929 host target gene. TOX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOX BINDING SITE, designated SEQ ID:16330, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64796] Another function of VGAM1929 is therefore inhibition of TOX (Accession NM\_014729). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOX. Tripartite Motif-containing 14 (TRIM14, Accession NM\_014788) is another VGAM1929 host target gene. TRIM14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM14 BINDING SITE, designated SEQ ID:16670, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ

ID:4640.

[64797] Another function of VGAM1929 is therefore inhibition of Tripartite Motif-containing 14 (TRIM14, Accession NM\_014788), a gene which is composed of 3 zinc-binding domains and is involved in development and cell growth. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM14. The function of TRIM14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Transient Receptor Potential Cation Channel, Subfamily C, Member 1 (TRPC1, Accession NM\_003304) is another VGAM1929 host target gene. TRPC1 BINDING SITE1 and TRPC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRPC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC1 BINDING SITE1 and TRPC1 BINDING SITE2, designated SEQ ID:9306 and SEQ ID:9308 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64798] Another function of VGAM1929 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 1 (TRPC1, Accession NM\_003304), a gene which acts as a non-voltage-sensitive store-operated  $\text{Ca}^{2+}$  channel. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC1. The function of TRPC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Translin (TSN, Accession NM\_004622) is another VGAM1929 host target gene. TSN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSN BINDING SITE, designated SEQ ID:10990, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64799] Another function of VGAM1929 is therefore inhibition of Translin (TSN, Accession NM\_004622), a gene which is a DNA binding protein and involved in DNA repair, replica-



tion, or recombination. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSN. The function of TSN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM98. Thioredoxin Reductase 1 (TXNRD1, Accession NM\_003330) is another VGAM1929 host target gene. TXNRD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TXNRD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TXNRD1 BINDING SITE, designated SEQ ID:9338, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64800] Another function of VGAM1929 is therefore inhibition of Thioredoxin Reductase 1 (TXNRD1, Accession NM\_003330), a gene which acts as an antioxidant enzyme and is involved in maintaining redox balance. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with TXNRD1. The function of TXNRD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Tyrosinase-related Protein 1 (TYRP1, Accession XM\_051267) is another VGAM1929 host target gene. TYRP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TYRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TYRP1 BINDING SITE, designated SEQ ID:35796, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64801] Another function of VGAM1929 is therefore inhibition of Tyrosinase-related Protein 1 (TYRP1, Accession XM\_051267). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TYRP1. Ubiquitin Protein Ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome) (UBE3A, Accession NM\_130839) is another VGAM1929 host target gene. UBE3A BINDING SITE1 through UBE3A BINDING SITE3 are HOST TARGET

binding sites found in untranslated regions of mRNA encoded by UBE3A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE3A BINDING SITE1 through UBE3A BINDING SITE3, designated SEQ ID:28366, SEQ ID:28362 and SEQ ID:6081 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64802] Another function of VGAM1929 is therefore inhibition of Ubiquitin Protein Ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome) (UBE3A, Accession NM\_130839). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE3A. Uracil-DNA Glycosylase (UNG, Accession NM\_003362) is another VGAM1929 host target gene. UNG BINDING SITE1 and UNG BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UNG, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UNG BINDING SITE1 and UNG BINDING SITE2, designated

SEQ ID:9389 and SEQ ID:9416 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64803] Another function of VGAM1929 is therefore inhibition of Uracil–DNA Glycosylase (UNG, Accession NM\_003362), a gene which excises uracil residues from the dna to prevent mutagenesis and initiate the base–excision repair (BER) pathway. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNG. The function of UNG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206.Xylulokinase Homolog (H. influenzae) (XYLB, Accession NM\_005108) is another VGAM1929 host target gene. XYLB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by XYLB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XYLB BINDING SITE, designated SEQ ID:11584, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64804] Another function of VGAM1929 is therefore inhibition of Xylulokinase Homolog (*H. influenzae*) (XYLB, Accession NM\_005108), a gene which is similar to *Haemophilus influenzae* xylulokinase and may play a role in energy metabolism. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XYLB. The function of XYLB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM127. Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Gamma Polypeptide (YWHAG, Accession NM\_012479) is another VGAM1929 host target gene. YWHAG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YWHAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YWHAG BINDING SITE, designated SEQ ID:14854, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64805] Another function of VGAM1929 is therefore inhibition of

Tyrosine 3-monooxygenase/tryptophan

5-monooxygenase Activation Protein, Gamma Polypeptide (YWHAG, Accession NM\_012479), a gene which mediates mitogenic signals of PDGF in vascular smooth muscle cells. Accordingly, utilities of VGAM1929 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with YWHAG. The function of YWHAG

and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Tyrosine

3-monooxygenase/tryptophan 5-monooxygenase Activa-

tion Protein, Eta Polypeptide (YWHAH, Accession

NM\_003405) is another VGAM1929 host target gene.

YWHAH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

YWHAH, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of YWHAH BINDING SITE, designated SEQ

ID:9441, to the nucleotide sequence of VGAM1929 RNA,

herein designated VGAM RNA, also designated SEQ

ID:4640.

[64806] Another function of VGAM1929 is therefore inhibition of

Tyrosine 3-monooxygenase/tryptophan

5-monooxygenase Activation Protein, Eta Polypeptide

(YWHAH, Accession NM\_003405), a gene which activates tyrosine and tryptophan hydroxylases in the presence of and strongly activates protein kinase c. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YWHAH. The function of YWHAH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1923. Zinc-fingers and Homeoboxes 1 (ZHX1, Accession NM\_007222) is another VGAM1929 host target gene. ZHX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZHX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZHX1 BINDING SITE, designated SEQ ID:14093, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64807] Another function of VGAM1929 is therefore inhibition of Zinc-fingers and Homeoboxes 1 (ZHX1, Accession

NM\_007222). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZHX1. Zinc Finger Protein 36 (KOX 18) (ZNF36, Accession XM\_168302) is another VGAM1929 host target gene. ZNF36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF36 BINDING SITE, designated SEQ ID:45104, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64808] Another function of VGAM1929 is therefore inhibition of Zinc Finger Protein 36 (KOX 18) (ZNF36, Accession XM\_168302), a gene which may be involved in transcriptional regulation. Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF36. The function of ZNF36 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM804. Zinc Finger Protein 80 (pT17) (ZNF80, Accession NM\_007136)



is another VGAM1929 host target gene. ZNF80 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF80, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF80 BINDING SITE, designated SEQ ID:13988, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64809] Another function of VGAM1929 is therefore inhibition of Zinc Finger Protein 80 (pT17) (ZNF80, Accession NM\_007136). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF80. ACP33 (Accession NM\_016630) is another VGAM1929 host target gene. ACP33 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ACP33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACP33 BINDING SITE, designated SEQ ID:18744, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ

ID:4640.

[64810] Another function of VGAM1929 is therefore inhibition of ACP33 (Accession NM\_016630). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACP33. AF311304 (Accession NM\_031214) is another VGAM1929 host target gene. AF311304 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AF311304, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AF311304 BINDING SITE, designated SEQ ID:25260, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64811] Another function of VGAM1929 is therefore inhibition of AF311304 (Accession NM\_031214). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AF311304. Agmatine Ureohydrolase (agmatinase) (AGMAT, Accession NM\_024758) is another VGAM1929 host target gene. AGMAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by AGMAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGMAT BINDING SITE, designated SEQ ID:24107, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64812] Another function of VGAM1929 is therefore inhibition of Agmatine Ureohydrolase (agmatinase) (AGMAT, Accession NM\_024758). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGMAT. A Kinase (PRKA) Anchor Protein 8 (AKAP8, Accession NM\_005858) is another VGAM1929 host target gene. AKAP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP8 BINDING SITE, designated SEQ ID:12464, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64813] Another function of VGAM1929 is therefore inhibition of A

Kinase (PRKA) Anchor Protein 8 (AKAP8, Accession NM\_005858). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP8. Adaptor-related Protein Complex 3, Mu 2 Subunit (AP3M2, Accession NM\_006803) is another VGAM1929 host target gene. AP3M2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP3M2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP3M2 BINDING SITE, designated SEQ ID:13679, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64814] Another function of VGAM1929 is therefore inhibition of Adaptor-related Protein Complex 3, Mu 2 Subunit (AP3M2, Accession NM\_006803). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP3M2. Apolipoprotein L, 4 (APOL4, Accession NM\_030643) is another VGAM1929 host target gene. APOL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by APOL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL4 BINDING SITE, designated SEQ ID:24979, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64815] Another function of VGAM1929 is therefore inhibition of Apolipoprotein L, 4 (APOL4, Accession NM\_030643). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL4. Ras Homolog Gene Family, Member E (ARHE, Accession NM\_005168) is another VGAM1929 host target gene. ARHE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHE BINDING SITE, designated SEQ ID:11669, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64816] Another function of VGAM1929 is therefore inhibition of

Ras Homolog Gene Family, Member E (ARHE, Accession NM\_005168). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHE. Rho Guanine Nucleotide Exchange Factor (GEF) 3 (ARHGEF3, Accession NM\_019555) is another VGAM1929 host target gene. ARHGEF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF3 BINDING SITE, designated SEQ ID:21209, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64817] Another function of VGAM1929 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 3 (ARHGEF3, Accession NM\_019555). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF3. Cdc42 Guanine Nucleotide Exchange Factor (GEF) 9 (ARHGEF9, Accession NM\_015185) is another VGAM1929 host target gene. ARHGEF9 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARHGEF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF9 BINDING SITE, designated SEQ ID:17540, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64818] Another function of VGAM1929 is therefore inhibition of Cdc42 Guanine Nucleotide Exchange Factor (GEF) 9 (ARHGEF9, Accession NM\_015185). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF9. ARL8 (Accession XM\_167671) is another VGAM1929 host target gene. ARL8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARL8 BINDING SITE, designated SEQ ID:44762, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64819] Another function of VGAM1929 is therefore inhibition of ARL8 (Accession XM\_167671). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARL8. ARNTL2 (Accession NM\_020183) is another VGAM1929 host target gene. ARNTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARNTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNTL2 BINDING SITE, designated SEQ ID:21413, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64820] Another function of VGAM1929 is therefore inhibition of ARNTL2 (Accession NM\_020183). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNTL2. ATPase, Class V, Type 10B (ATP10B, Accession XM\_032721) is another VGAM1929 host target gene. ATP10B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP10B, corresponding to a HOST TARGET binding site



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP10B BINDING SITE, designated SEQ ID:31737, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64821] Another function of VGAM1929 is therefore inhibition of ATPase, Class V, Type 10B (ATP10B, Accession XM\_032721). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP10B. ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577) is another VGAM1929 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31087, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64822] Another function of VGAM1929 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577).

Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. BCMP1 (Accession NM\_031442) is another VGAM1929 host target gene. BCMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCMP1 BINDING SITE, designated SEQ ID:25456, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64823] Another function of VGAM1929 is therefore inhibition of BCMP1 (Accession NM\_031442). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCMP1. Chromosome 12 Open Reading Frame 22 (C12orf22, Accession NM\_030809) is another VGAM1929 host target gene. C12orf22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C12orf22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C12orf22 BINDING SITE, designated SEQ ID:25126, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64824] Another function of VGAM1929 is therefore inhibition of Chromosome 12 Open Reading Frame 22 (C12orf22, Accession NM\_030809). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C12orf22. Chromosome 13 Open Reading Frame 1 (C13orf1, Accession NM\_020456) is another VGAM1929 host target gene. C13orf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C13orf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C13orf1 BINDING SITE, designated SEQ ID:21691, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64825] Another function of VGAM1929 is therefore inhibition of Chromosome 13 Open Reading Frame 1 (C13orf1, Acces-

sion NM\_020456). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf1. Chromosome 1 Open Reading Frame 22 (C1orf22, Accession NM\_025191) is another VGAM1929 host target gene. C1orf22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf22 BINDING SITE, designated SEQ ID:24839, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64826] Another function of VGAM1929 is therefore inhibition of Chromosome 1 Open Reading Frame 22 (C1orf22, Accession NM\_025191). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf22. Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM\_052966) is another VGAM1929 host target gene. C1orf24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

C1orf24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf24 BINDING SITE, designated SEQ ID:27532, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64827] Another function of VGAM1929 is therefore inhibition of Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM\_052966). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf24. Chromosome 20 Open Reading Frame 130 (C20orf130, Accession XM\_029741) is another VGAM1929 host target gene. C20orf130 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf130 BINDING SITE, designated SEQ ID:30938, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64828] Another function of VGAM1929 is therefore inhibition of Chromosome 20 Open Reading Frame 130 (C20orf130, Accession XM\_029741). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf130. Chromosome 21 Open Reading Frame 41 (C21orf41, Accession NM\_138332) is another VGAM1929 host target gene. C21orf41 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf41, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf41 BINDING SITE, designated SEQ ID:28730, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64829] Another function of VGAM1929 is therefore inhibition of Chromosome 21 Open Reading Frame 41 (C21orf41, Accession NM\_138332). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf41. Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM\_016605) is another VGAM1929 host target gene.

C5orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C5orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf6 BINDING SITE, designated SEQ ID:18702, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64830] Another function of VGAM1929 is therefore inhibition of Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM\_016605). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf6. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294) is another VGAM1929 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26070, to the nucleotide sequence of

VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64831] Another function of VGAM1929 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM\_032294). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM\_031409) is another VGAM1929 host target gene. CCR6 BINDING SITE1 and CCR6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCR6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR6 BINDING SITE1 and CCR6 BINDING SITE2, designated SEQ ID:25373 and SEQ ID:10579 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64832] Another function of VGAM1929 is therefore inhibition of Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM\_031409). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical



cal conditions associated with CCR6. CHFR (Accession NM\_018223) is another VGAM1929 host target gene. CHFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHFR BINDING SITE, designated SEQ ID:20150, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64833] Another function of VGAM1929 is therefore inhibition of CHFR (Accession NM\_018223). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHFR. Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 4 (CHST4, Accession NM\_005769) is another VGAM1929 host target gene. CHST4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHST4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST4 BINDING SITE, designated SEQ ID:12340, to the nucleotide sequence of

VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64834] Another function of VGAM1929 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 4 (CHST4, Accession NM\_005769). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST4. Carbohydrate (chondroitin) Synthase 1 (CHSY1, Accession NM\_014918) is another VGAM1929 host target gene. CHSY1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHSY1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHSY1 BINDING SITE, designated SEQ ID:17173, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64835] Another function of VGAM1929 is therefore inhibition of Carbohydrate (chondroitin) Synthase 1 (CHSY1, Accession NM\_014918). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHSY1. Cytoskeleton-associ-

ated Protein 4 (CKAP4, Accession NM\_006825) is another VGAM1929 host target gene. CKAP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKAP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKAP4 BINDING SITE, designated SEQ ID:13705, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64836] Another function of VGAM1929 is therefore inhibition of Cytoskeleton-associated Protein 4 (CKAP4, Accession NM\_006825). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKAP4. Claudin 4 (CLDN4, Accession NM\_001305) is another VGAM1929 host target gene. CLDN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLDN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLDN4 BINDING SITE, designated SEQ ID:6988, to the nucleotide sequence of VGAM1929 RNA,

herein designated VGAM RNA, also designated SEQ ID:4640.

[64837] Another function of VGAM1929 is therefore inhibition of Claudin 4 (CLDN4, Accession NM\_001305). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLDN4. Crn, Crooked Neck-like 1 (Drosophila) (CRNKL1, Accession NM\_016652) is another VGAM1929 host target gene. CRNKL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRNKL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRNKL1 BINDING SITE, designated SEQ ID:18774, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64838] Another function of VGAM1929 is therefore inhibition of Crn, Crooked Neck-like 1 (Drosophila) (CRNKL1, Accession NM\_016652). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRNKL1. CTP Synthase II (CTPS2, Accession NM\_019857) is another VGAM1929

host target gene. CTPS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTPS2 BINDING SITE, designated SEQ ID:21262, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64839] Another function of VGAM1929 is therefore inhibition of CTP Synthase II (CTPS2, Accession NM\_019857). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTPS2. D2S448 (Accession XM\_056455) is another VGAM1929 host target gene. D2S448 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by D2S448, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D2S448 BINDING SITE, designated SEQ ID:36395, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64840] Another function of VGAM1929 is therefore inhibition of D2S448 (Accession XM\_056455). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D2S448. DJ971N18.2 (Accession NM\_021156) is another VGAM1929 host target gene. DJ971N18.2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ971N18.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ971N18.2 BINDING SITE, designated SEQ ID:22134, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64841] Another function of VGAM1929 is therefore inhibition of DJ971N18.2 (Accession NM\_021156). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ971N18.2. DKFZP434C0826 (Accession XM\_097248) is another VGAM1929 host target gene. DKFZP434C0826 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434C0826, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C0826 BINDING SITE, designated SEQ ID:40844, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64842] Another function of VGAM1929 is therefore inhibition of DKFZP434C0826 (Accession XM\_097248). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C0826. DKFZP434D1335 (Accession XM\_036578) is another VGAM1929 host target gene. DKFZP434D1335 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434D1335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434D1335 BINDING SITE, designated SEQ ID:32468, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64843] Another function of VGAM1929 is therefore inhibition of DKFZP434D1335 (Accession XM\_036578). Accordingly,

utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434D1335. DKFZp434D177 (Accession NM\_032264) is another VGAM1929 host target gene. DKFZp434D177 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434D177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434D177 BINDING SITE, designated SEQ ID:26010, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64844] Another function of VGAM1929 is therefore inhibition of DKFZp434D177 (Accession NM\_032264). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434D177. DKFZP434J1813 (Accession XM\_029798) is another VGAM1929 host target gene. DKFZP434J1813 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434J1813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-



ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434J1813 BINDING SITE, designated SEQ ID:30949, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64845] Another function of VGAM1929 is therefore inhibition of DKFZP434J1813 (Accession XM\_029798). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434J1813. DKFZP434O125 (Accession XM\_036284) is another VGAM1929 host target gene. DKFZP434O125 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434O125, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434O125 BINDING SITE, designated SEQ ID:32407, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64846] Another function of VGAM1929 is therefore inhibition of DKFZP434O125 (Accession XM\_036284). Accordingly, utilities of VGAM1929 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP434O125. DKFZp547I224 (Accession NM\_020221) is another VGAM1929 host target gene. DKFZp547I224 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp547I224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I224 BINDING SITE, designated SEQ ID:21477, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64847] Another function of VGAM1929 is therefore inhibition of DKFZp547I224 (Accession NM\_020221). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547I224. DKFZP564I0422 (Accession NM\_031435) is another VGAM1929 host target gene. DKFZP564I0422 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564I0422, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of DKFZP564I0422 BINDING SITE, designated SEQ ID:25434, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64848] Another function of VGAM1929 is therefore inhibition of DKFZP564I0422 (Accession NM\_031435). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I0422. DKFZP564L2423 (Accession XM\_031015) is another VGAM1929 host target gene. DKFZP564L2423 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564L2423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564L2423 BINDING SITE, designated SEQ ID:31259, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64849] Another function of VGAM1929 is therefore inhibition of DKFZP564L2423 (Accession XM\_031015). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZP564L2423. DKFZP564O0823 (Accession XM\_003517) is another VGAM1929 host target gene. DKFZP564O0823 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O0823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0823 BINDING SITE, designated SEQ ID:29938, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64850] Another function of VGAM1929 is therefore inhibition of DKFZP564O0823 (Accession XM\_003517). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0823. DKFZp566H0824 (Accession NM\_017535) is another VGAM1929 host target gene. DKFZp566H0824 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp566H0824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp566H0824 BINDING SITE,

designated SEQ ID:18979, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64851] Another function of VGAM1929 is therefore inhibition of DKFZp566H0824 (Accession NM\_017535). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp566H0824. DKFZP727C091 (Accession XM\_038689) is another VGAM1929 host target gene. DKFZP727C091 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP727C091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP727C091 BINDING SITE, designated SEQ ID:32905, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64852] Another function of VGAM1929 is therefore inhibition of DKFZP727C091 (Accession XM\_038689). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP727C091. DKFZp761D0614 (Accession

XM\_113634) is another VGAM1929 host target gene. DKFZp761D0614 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761D0614, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761D0614 BINDING SITE, designated SEQ ID:42310, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64853] Another function of VGAM1929 is therefore inhibition of DKFZp761D0614 (Accession XM\_113634). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761D0614. DKFZP761F241 (Accession NM\_031455) is another VGAM1929 host target gene. DKFZP761F241 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP761F241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP761F241 BINDING SITE, designated SEQ ID:25478, to the nucleotide sequence of

VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64854] Another function of VGAM1929 is therefore inhibition of DKFZP761F241 (Accession NM\_031455). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761F241. DnaJ (Hsp40) Homolog, Subfamily A, Member 4 (DNAJA4, Accession NM\_018602) is another VGAM1929 host target gene. DNAJA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJA4 BINDING SITE, designated SEQ ID:20679, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64855] Another function of VGAM1929 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily A, Member 4 (DNAJA4, Accession NM\_018602). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJA4. DnaJ (Hsp40) Homolog, Subfamily C, Member 6

(DNAJC6, Accession NM\_014787) is another VGAM1929 host target gene. DNAJC6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DNAJC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJC6 BINDING SITE, designated SEQ ID:16663, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64856] Another function of VGAM1929 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily C, Member 6 (DNAJC6, Accession NM\_014787). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJC6. Dual Specificity Phosphatase 9 (DUSP9, Accession NM\_001395) is another VGAM1929 host target gene. DUSP9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DUSP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP9 BINDING SITE, designated SEQ ID:7091,



to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64857] Another function of VGAM1929 is therefore inhibition of Dual Specificity Phosphatase 9 (DUSP9, Accession NM\_001395). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DUSP9. Eukaryotic Translation Initiation Factor 5 (EIF5, Accession NM\_001969) is another VGAM1929 host target gene. EIF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF5 BINDING SITE, designated SEQ ID:7702, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64858] Another function of VGAM1929 is therefore inhibition of Eukaryotic Translation Initiation Factor 5 (EIF5, Accession NM\_001969). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF5. Elac Homolog 1 (E. coli) (ELAC1, Accession XM\_165659) is another

VGAM1929 host target gene. ELAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELAC1 BINDING SITE, designated SEQ ID:43723, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64859] Another function of VGAM1929 is therefore inhibition of ElaC Homolog 1 (E. coli) (ELAC1, Accession XM\_165659). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELAC1. E74-like Factor 4 (ets domain transcription factor) (ELF4, Accession NM\_001421) is another VGAM1929 host target gene. ELF4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELF4 BINDING SITE, designated SEQ ID:7128, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also

designated SEQ ID:4640.

[64860] Another function of VGAM1929 is therefore inhibition of E74-like Factor 4 (ets domain transcription factor) (ELF4, Accession NM\_001421). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELF4. ESDN (Accession NM\_080927) is another VGAM1929 host target gene. ESDN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESDN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESDN BINDING SITE, designated SEQ ID:28152, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64861] Another function of VGAM1929 is therefore inhibition of ESDN (Accession NM\_080927). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESDN. Ecotropic Viral Integration Site 5 (EVI5, Accession NM\_005665) is another VGAM1929 host target gene. EVI5 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by EVI5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVI5 BINDING SITE, designated SEQ ID:12209, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64862] Another function of VGAM1929 is therefore inhibition of Ecotropic Viral Integration Site 5 (EVI5, Accession NM\_005665). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVI5. FLJ10292 (Accession NM\_018048) is another VGAM1929 host target gene. FLJ10292 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10292 BINDING SITE, designated SEQ ID:19803, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64863] Another function of VGAM1929 is therefore inhibition of

FLJ10292 (Accession NM\_018048). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10292. FLJ10493 (Accession NM\_018112) is another VGAM1929 host target gene. FLJ10493 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10493 BINDING SITE, designated SEQ ID:19885, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64864] Another function of VGAM1929 is therefore inhibition of FLJ10493 (Accession NM\_018112). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10493. FLJ10546 (Accession XM\_002989) is another VGAM1929 host target gene. FLJ10546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ10546 BINDING SITE, designated SEQ ID:29913, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64865] Another function of VGAM1929 is therefore inhibition of FLJ10546 (Accession XM\_002989). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10546. FLJ10726 (Accession NM\_018195) is another VGAM1929 host target gene. FLJ10726 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10726, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10726 BINDING SITE, designated SEQ ID:20061, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64866] Another function of VGAM1929 is therefore inhibition of FLJ10726 (Accession NM\_018195). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10726. FLJ10803 (Accession NM\_018224) is another

VGAM1929 host target gene. FLJ10803 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10803, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10803 BINDING SITE, designated SEQ ID:20154, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64867] Another function of VGAM1929 is therefore inhibition of FLJ10803 (Accession NM\_018224). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10803. FLJ10852 (Accession NM\_019028) is another VGAM1929 host target gene. FLJ10852 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10852, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10852 BINDING SITE, designated SEQ ID:21119, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64868] Another function of VGAM1929 is therefore inhibition of FLJ10852 (Accession NM\_019028). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10852. FLJ10996 (Accession NM\_019044) is another VGAM1929 host target gene. FLJ10996 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10996, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10996 BINDING SITE, designated SEQ ID:21128, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64869] Another function of VGAM1929 is therefore inhibition of FLJ10996 (Accession NM\_019044). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10996. FLJ11184 (Accession NM\_018352) is another VGAM1929 host target gene. FLJ11184 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11184, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11184 BINDING SITE, designated SEQ ID:20365, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64870] Another function of VGAM1929 is therefore inhibition of FLJ11184 (Accession NM\_018352). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11184. FLJ12154 (Accession NM\_021944) is another VGAM1929 host target gene. FLJ12154 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12154 BINDING SITE, designated SEQ ID:22464, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64871] Another function of VGAM1929 is therefore inhibition of FLJ12154 (Accession NM\_021944). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ12154. FLJ12425 (Accession XM\_098290) is another VGAM1929 host target gene. FLJ12425 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12425 BINDING SITE, designated SEQ ID:41565, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64872] Another function of VGAM1929 is therefore inhibition of FLJ12425 (Accession XM\_098290). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12425. FLJ12443 (Accession NM\_024830) is another VGAM1929 host target gene. FLJ12443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12443 BINDING SITE, designated SEQ ID:24226, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM

RNA, also designated SEQ ID:4640.

[64873] Another function of VGAM1929 is therefore inhibition of FLJ12443 (Accession NM\_024830). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12443. FLJ12581 (Accession NM\_024865) is another VGAM1929 host target gene. FLJ12581 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ12581, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12581 BINDING SITE, designated SEQ ID:24302, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64874] Another function of VGAM1929 is therefore inhibition of FLJ12581 (Accession NM\_024865). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12581. FLJ12770 (Accession NM\_032174) is another VGAM1929 host target gene. FLJ12770 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12770, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12770 BINDING SITE, designated SEQ ID:25888, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64875] Another function of VGAM1929 is therefore inhibition of FLJ12770 (Accession NM\_032174). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12770. FLJ12895 (Accession NM\_023926) is another VGAM1929 host target gene. FLJ12895 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12895 BINDING SITE, designated SEQ ID:23406, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64876] Another function of VGAM1929 is therefore inhibition of FLJ12895 (Accession NM\_023926). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ12895. FLJ12903 (Accession NM\_022753) is another VGAM1929 host target gene. FLJ12903 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12903, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12903 BINDING SITE, designated SEQ ID:22981, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64877] Another function of VGAM1929 is therefore inhibition of FLJ12903 (Accession NM\_022753). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12903. FLJ13213 (Accession NM\_024755) is another VGAM1929 host target gene. FLJ13213 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13213 BINDING SITE, designated SEQ ID:24100, to the nucleotide

sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64878] Another function of VGAM1929 is therefore inhibition of FLJ13213 (Accession NM\_024755). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13213. FLJ13315 (Accession NM\_025005) is another VGAM1929 host target gene. FLJ13315 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13315, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13315 BINDING SITE, designated SEQ ID:24578, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64879] Another function of VGAM1929 is therefore inhibition of FLJ13315 (Accession NM\_025005). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13315. FLJ13646 (Accession NM\_024584) is another VGAM1929 host target gene. FLJ13646 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ13646, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13646 BINDING SITE, designated SEQ ID:23817, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64880] Another function of VGAM1929 is therefore inhibition of FLJ13646 (Accession NM\_024584). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13646. FLJ13842 (Accession NM\_024645) is another VGAM1929 host target gene. FLJ13842 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13842 BINDING SITE, designated SEQ ID:23931, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64881] Another function of VGAM1929 is therefore inhibition of FLJ13842 (Accession NM\_024645). Accordingly, utilities of

VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13842. FLJ14466 (Accession NM\_032790) is another VGAM1929 host target gene. FLJ14466 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14466 BINDING SITE, designated SEQ ID:26544, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64882] Another function of VGAM1929 is therefore inhibition of FLJ14466 (Accession NM\_032790). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14466. FLJ14564 (Accession XM\_084459) is another VGAM1929 host target gene. FLJ14564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14564



BINDING SITE, designated SEQ ID:37597, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64883] Another function of VGAM1929 is therefore inhibition of FLJ14564 (Accession XM\_084459). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14564. FLJ14621 (Accession NM\_032811) is another VGAM1929 host target gene. FLJ14621 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14621, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14621 BINDING SITE, designated SEQ ID:26583, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64884] Another function of VGAM1929 is therefore inhibition of FLJ14621 (Accession NM\_032811). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14621. FLJ20232 (Accession NM\_019008) is another VGAM1929 host target gene. FLJ20232 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20232 BINDING SITE, designated SEQ ID:21084, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64885] Another function of VGAM1929 is therefore inhibition of FLJ20232 (Accession NM\_019008). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20232. FLJ20273 (Accession NM\_019027) is another VGAM1929 host target gene. FLJ20273 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20273 BINDING SITE, designated SEQ ID:21116, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64886] Another function of VGAM1929 is therefore inhibition of

FLJ20273 (Accession NM\_019027). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20273. FLJ20337 (Accession NM\_017772) is another VGAM1929 host target gene. FLJ20337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20337 BINDING SITE, designated SEQ ID:19393, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64887] Another function of VGAM1929 is therefore inhibition of FLJ20337 (Accession NM\_017772). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20337. FLJ20508 (Accession NM\_017850) is another VGAM1929 host target gene. FLJ20508 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ20508 BINDING SITE, designated SEQ ID:19520, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64888] Another function of VGAM1929 is therefore inhibition of FLJ20508 (Accession NM\_017850). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20508. FLJ20509 (Accession NM\_017851) is another VGAM1929 host target gene. FLJ20509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20509 BINDING SITE, designated SEQ ID:19524, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64889] Another function of VGAM1929 is therefore inhibition of FLJ20509 (Accession NM\_017851). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20509. FLJ20542 (Accession NM\_032179) is another

VGAM1929 host target gene. FLJ20542 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20542, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20542 BINDING SITE, designated SEQ ID:25893, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64890] Another function of VGAM1929 is therefore inhibition of FLJ20542 (Accession NM\_032179). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20542. FLJ20666 (Accession NM\_018333) is another VGAM1929 host target gene. FLJ20666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20666 BINDING SITE, designated SEQ ID:20338, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64891] Another function of VGAM1929 is therefore inhibition of FLJ20666 (Accession NM\_018333). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20666. FLJ20700 (Accession NM\_017932) is another VGAM1929 host target gene. FLJ20700 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20700 BINDING SITE, designated SEQ ID:19620, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64892] Another function of VGAM1929 is therefore inhibition of FLJ20700 (Accession NM\_017932). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20700. FLJ20793 (Accession XM\_166296) is another VGAM1929 host target gene. FLJ20793 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20793, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20793 BINDING SITE, designated SEQ ID:44109, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64893] Another function of VGAM1929 is therefore inhibition of FLJ20793 (Accession XM\_166296). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20793. FLJ20972 (Accession NM\_025030) is another VGAM1929 host target gene. FLJ20972 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20972, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20972 BINDING SITE, designated SEQ ID:24626, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64894] Another function of VGAM1929 is therefore inhibition of FLJ20972 (Accession NM\_025030). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ20972. FLJ21032 (Accession NM\_024906) is another VGAM1929 host target gene. FLJ21032 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21032 BINDING SITE, designated SEQ ID:24400, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64895] Another function of VGAM1929 is therefore inhibition of FLJ21032 (Accession NM\_024906). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21032. FLJ21477 (Accession NM\_025153) is another VGAM1929 host target gene. FLJ21477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21477 BINDING SITE, designated SEQ ID:24790, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM



RNA, also designated SEQ ID:4640.

[64896] Another function of VGAM1929 is therefore inhibition of FLJ21477 (Accession NM\_025153). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21477. FLJ21551 (Accession NM\_024801) is another VGAM1929 host target gene. FLJ21551 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21551, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21551 BINDING SITE, designated SEQ ID:24179, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64897] Another function of VGAM1929 is therefore inhibition of FLJ21551 (Accession NM\_024801). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21551. FLJ21615 (Accession NM\_032205) is another VGAM1929 host target gene. FLJ21615 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21615, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21615 BINDING SITE, designated SEQ ID:25910, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64898] Another function of VGAM1929 is therefore inhibition of FLJ21615 (Accession NM\_032205). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21615. FLJ21777 (Accession NM\_032209) is another VGAM1929 host target gene. FLJ21777 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21777, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21777 BINDING SITE, designated SEQ ID:25925, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64899] Another function of VGAM1929 is therefore inhibition of FLJ21777 (Accession NM\_032209). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ21777. FLJ22028 (Accession NM\_024854) is another VGAM1929 host target gene. FLJ22028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22028 BINDING SITE, designated SEQ ID:24285, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64900] Another function of VGAM1929 is therefore inhibition of FLJ22028 (Accession NM\_024854). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22028. FLJ22055 (Accession NM\_024779) is another VGAM1929 host target gene. FLJ22055 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22055, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22055 BINDING SITE, designated SEQ ID:24148, to the nucleotide

sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64901] Another function of VGAM1929 is therefore inhibition of FLJ22055 (Accession NM\_024779). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22055. FLJ22169 (Accession NM\_024085) is another VGAM1929 host target gene. FLJ22169 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22169, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22169 BINDING SITE, designated SEQ ID:23522, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64902] Another function of VGAM1929 is therefore inhibition of FLJ22169 (Accession NM\_024085). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22169. FLJ22724 (Accession NM\_024532) is another VGAM1929 host target gene. FLJ22724 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ22724, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22724 BINDING SITE, designated SEQ ID:23736, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64903] Another function of VGAM1929 is therefore inhibition of FLJ22724 (Accession NM\_024532). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22724. FLJ30058 (Accession NM\_144967) is another VGAM1929 host target gene. FLJ30058 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30058, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30058 BINDING SITE, designated SEQ ID:29583, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64904] Another function of VGAM1929 is therefore inhibition of FLJ30058 (Accession NM\_144967). Accordingly, utilities of

VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30058. Frequenin Homolog (Drosophila) (FREQ, Accession NM\_014286) is another VGAM1929 host target gene. FREQ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FREQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FREQ BINDING SITE, designated SEQ ID:15565, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64905] Another function of VGAM1929 is therefore inhibition of Frequenin Homolog (Drosophila) (FREQ, Accession NM\_014286). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FREQ. Far Upstream Element (FUSE) Binding Protein 3 (FUBP3, Accession XM\_033327) is another VGAM1929 host target gene. FUBP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of FUBP3 BINDING SITE, designated SEQ ID:31878, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64906] Another function of VGAM1929 is therefore inhibition of Far Upstream Element (FUSE) Binding Protein 3 (FUBP3, Accession XM\_033327). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUBP3. Fucosyltransferase 10 (alpha (1,3) Fucosyltransferase) (FUT10, Accession NM\_032664) is another VGAM1929 host target gene. FUT10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT10 BINDING SITE, designated SEQ ID:26394, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64907] Another function of VGAM1929 is therefore inhibition of Fucosyltransferase 10 (alpha (1,3) Fucosyltransferase)

(FUT10, Accession NM\_032664). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT10. G2 (Accession XM\_039515) is another VGAM1929 host target gene. G2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G2 BINDING SITE, designated SEQ ID:33111, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64908] Another function of VGAM1929 is therefore inhibition of G2 (Accession XM\_039515). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G2. Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM\_022130) is another VGAM1929 host target gene. GOLPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide



sequences of GOLPH3 BINDING SITE, designated SEQ ID:22690, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64909] Another function of VGAM1929 is therefore inhibition of Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM\_022130). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLPH3. G Protein-coupled Receptor 107 (GPR107, Accession NM\_020960) is another VGAM1929 host target gene. GPR107 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR107, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR107 BINDING SITE, designated SEQ ID:21949, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64910] Another function of VGAM1929 is therefore inhibition of G Protein-coupled Receptor 107 (GPR107, Accession NM\_020960). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with GPR107. GS3955 (Accession NM\_021643) is another VGAM1929 host target gene. GS3955 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GS3955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GS3955 BINDING SITE, designated SEQ ID:22307, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64911] Another function of VGAM1929 is therefore inhibition of GS3955 (Accession NM\_021643). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GS3955. H2AV (Accession NM\_138635) is another VGAM1929 host target gene. H2AV BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by H2AV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H2AV BINDING SITE, designated SEQ ID:28910, to the nucleotide sequence of

VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64912] Another function of VGAM1929 is therefore inhibition of H2AV (Accession NM\_138635). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H2AV. H326 (Accession NM\_015726) is another VGAM1929 host target gene. H326 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H326, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H326 BINDING SITE, designated SEQ ID:17941, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64913] Another function of VGAM1929 is therefore inhibition of H326 (Accession NM\_015726). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H326. HEMK (Accession NM\_016173) is another VGAM1929 host target gene. HEMK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by HEMK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEMK BINDING SITE, designated SEQ ID:18268, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64914] Another function of VGAM1929 is therefore inhibition of HEMK (Accession NM\_016173). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEMK. Heterogeneous Nuclear Ribonucleoprotein A3 (HNRPA3, Accession NM\_005758) is another VGAM1929 host target gene. HNRPA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPA3 BINDING SITE, designated SEQ ID:12326, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64915] Another function of VGAM1929 is therefore inhibition of

Heterogeneous Nuclear Ribonucleoprotein A3 (HNRPA3, Accession NM\_005758). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPA3. HOMER-2B (Accession NM\_004839) is another VGAM1929 host target gene. HOMER-2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOMER-2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOMER-2B BINDING SITE, designated SEQ ID:11247, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64916] Another function of VGAM1929 is therefore inhibition of HOMER-2B (Accession NM\_004839). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOMER-2B. HPIP (Accession NM\_020524) is another VGAM1929 host target gene. HPIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPIP BINDING SITE, designated SEQ ID:21737, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64917] Another function of VGAM1929 is therefore inhibition of HPIP (Accession NM\_020524). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPIP. HSA249128 (Accession NM\_017583) is another VGAM1929 host target gene. HSA249128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA249128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA249128 BINDING SITE, designated SEQ ID:19025, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64918] Another function of VGAM1929 is therefore inhibition of HSA249128 (Accession NM\_017583). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

HSA249128. HSA277841 (Accession NM\_018553) is another VGAM1929 host target gene. HSA277841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA277841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA277841 BINDING SITE, designated SEQ ID:20633, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64919] Another function of VGAM1929 is therefore inhibition of HSA277841 (Accession NM\_018553). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA277841. HSPC129 (Accession NM\_016396) is another VGAM1929 host target gene. HSPC129 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC129 BINDING SITE, designated SEQ ID:18535, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM

RNA, also designated SEQ ID:4640.

[64920] Another function of VGAM1929 is therefore inhibition of HSPC129 (Accession NM\_016396). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC129. Internexin Neuronal Intermediate Filament Protein, Alpha (INA, Accession NM\_032727) is another VGAM1929 host target gene. INA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INA BINDING SITE, designated SEQ ID:26453, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64921] Another function of VGAM1929 is therefore inhibition of Internexin Neuronal Intermediate Filament Protein, Alpha (INA, Accession NM\_032727). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INA. Inhibitor of Growth Family, Member 4 (ING4, Accession XM\_006980) is another VGAM1929 host target gene. ING4



BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ING4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ING4 BINDING SITE, designated SEQ ID:30026, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64922] Another function of VGAM1929 is therefore inhibition of Inhibitor of Growth Family, Member 4 (ING4, Accession XM\_006980). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ING4. K-ALPHA-1 (Accession XM\_084866) is another VGAM1929 host target gene. K-ALPHA-1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by K-ALPHA-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of K-ALPHA-1 BINDING SITE, designated SEQ ID:37742, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64923] Another function of VGAM1929 is therefore inhibition of K-ALPHA-1 (Accession XM\_084866). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with K-ALPHA-1. KIAA0087 (Accession NM\_014769) is another VGAM1929 host target gene. KIAA0087 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0087, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0087 BINDING SITE, designated SEQ ID:16560, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64924] Another function of VGAM1929 is therefore inhibition of KIAA0087 (Accession NM\_014769). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0087. KIAA0185 (Accession XM\_031992) is another VGAM1929 host target gene. KIAA0185 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0185, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0185 BINDING SITE, designated SEQ ID:31538, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64925] Another function of VGAM1929 is therefore inhibition of KIAA0185 (Accession XM\_031992). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0185. KIAA0186 (Accession NM\_021067) is another VGAM1929 host target gene. KIAA0186 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0186, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0186 BINDING SITE, designated SEQ ID:22038, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64926] Another function of VGAM1929 is therefore inhibition of KIAA0186 (Accession NM\_021067). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0186. KIAA0215 (Accession NM\_014735) is another VGAM1929 host target gene. KIAA0215 BINDING SITE1 and KIAA0215 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0215, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0215 BINDING SITE1 and KIAA0215 BINDING SITE2, designated SEQ ID:16383 and SEQ ID:16386 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64927] Another function of VGAM1929 is therefore inhibition of KIAA0215 (Accession NM\_014735). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0215. KIAA0255 (Accession NM\_014742) is another VGAM1929 host target gene. KIAA0255 BINDING SITE1 and KIAA0255 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0255, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of KIAA0255 BINDING SITE1 and KIAA0255 BINDING SITE2, designated SEQ ID:16418 and SEQ ID:34626 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64928] Another function of VGAM1929 is therefore inhibition of KIAA0255 (Accession NM\_014742). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0255. KIAA0318 (Accession XM\_044334) is another VGAM1929 host target gene. KIAA0318 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0318 BINDING SITE, designated SEQ ID:34190, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64929] Another function of VGAM1929 is therefore inhibition of KIAA0318 (Accession XM\_044334). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0318. KIAA0323 (Accession XM\_032634) is another VGAM1929 host target gene. KIAA0323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0323 BINDING SITE, designated SEQ ID:31693, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64930] Another function of VGAM1929 is therefore inhibition of KIAA0323 (Accession XM\_032634). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0323. KIAA0349 (Accession XM\_166449) is another VGAM1929 host target gene. KIAA0349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0349 BINDING SITE, designated SEQ ID:44343, to the nucleotide sequence of VGAM1929 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4640.

[64931] Another function of VGAM1929 is therefore inhibition of KIAA0349 (Accession XM\_166449). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0349. KIAA0417 (Accession XM\_048898) is another VGAM1929 host target gene. KIAA0417 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0417, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0417 BINDING SITE, designated SEQ ID:35290, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64932] Another function of VGAM1929 is therefore inhibition of KIAA0417 (Accession XM\_048898). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0417. KIAA0431 (Accession NM\_015251) is another VGAM1929 host target gene. KIAA0431 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0431, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0431 BINDING SITE, designated SEQ ID:17579, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64933] Another function of VGAM1929 is therefore inhibition of KIAA0431 (Accession NM\_015251). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0431. KIAA0435 (Accession NM\_014801) is another VGAM1929 host target gene. KIAA0435 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0435 BINDING SITE, designated SEQ ID:16719, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64934] Another function of VGAM1929 is therefore inhibition of KIAA0435 (Accession NM\_014801). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with KIAA0435. KIAA0446 (Accession XM\_044155) is another VGAM1929 host target gene. KIAA0446 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0446, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0446 BINDING SITE, designated SEQ ID:34156, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64935] Another function of VGAM1929 is therefore inhibition of KIAA0446 (Accession XM\_044155). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0446. KIAA0494 (Accession NM\_014774) is another VGAM1929 host target gene. KIAA0494 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0494 BINDING SITE, designated SEQ ID:16594, to the

nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64936] Another function of VGAM1929 is therefore inhibition of KIAA0494 (Accession NM\_014774). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0494. KIAA0515 (Accession XM\_033380) is another VGAM1929 host target gene. KIAA0515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0515 BINDING SITE, designated SEQ ID:31923, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64937] Another function of VGAM1929 is therefore inhibition of KIAA0515 (Accession XM\_033380). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0515. KIAA0522 (Accession XM\_050404) is another VGAM1929 host target gene. KIAA0522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0522 BINDING SITE, designated SEQ ID:35623, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64938] Another function of VGAM1929 is therefore inhibition of KIAA0522 (Accession XM\_050404). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0522. KIAA0682 (Accession NM\_014852) is another VGAM1929 host target gene. KIAA0682 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0682 BINDING SITE, designated SEQ ID:16902, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64939] Another function of VGAM1929 is therefore inhibition of KIAA0682 (Accession NM\_014852). Accordingly, utilities

of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0682. KIAA0802 (Accession XM\_031357) is another VGAM1929 host target gene. KIAA0802 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0802, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0802 BINDING SITE, designated SEQ ID:31354, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64940] Another function of VGAM1929 is therefore inhibition of KIAA0802 (Accession XM\_031357). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0802. KIAA0825 (Accession XM\_027906) is another VGAM1929 host target gene. KIAA0825 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0825, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0825 BINDING SITE, designated SEQ ID:30595, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64941] Another function of VGAM1929 is therefore inhibition of KIAA0825 (Accession XM\_027906). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0825. KIAA0844 (Accession NM\_014951) is another VGAM1929 host target gene. KIAA0844 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0844, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0844 BINDING SITE, designated SEQ ID:17286, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64942] Another function of VGAM1929 is therefore inhibition of KIAA0844 (Accession NM\_014951). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0844. KIAA0848 (Accession NM\_014926) is another VGAM1929 host target gene. KIAA0848 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0848 BINDING SITE, designated SEQ ID:17215, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64943] Another function of VGAM1929 is therefore inhibition of KIAA0848 (Accession NM\_014926). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0848. KIAA0854 (Accession NM\_014943) is another VGAM1929 host target gene. KIAA0854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0854 BINDING SITE, designated SEQ ID:17254, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64944] Another function of VGAM1929 is therefore inhibition of

KIAA0854 (Accession NM\_014943). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0854. KIAA0865 (Accession XM\_028522) is another VGAM1929 host target gene. KIAA0865 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0865 BINDING SITE, designated SEQ ID:30712, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64945] Another function of VGAM1929 is therefore inhibition of KIAA0865 (Accession XM\_028522). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0865. KIAA0882 (Accession XM\_093895) is another VGAM1929 host target gene. KIAA0882 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0882, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0882 BINDING SITE, designated SEQ ID:40217, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64946] Another function of VGAM1929 is therefore inhibition of KIAA0882 (Accession XM\_093895). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0882. KIAA0894 (Accession NM\_014896) is another VGAM1929 host target gene. KIAA0894 BINDING SITE1 and KIAA0894 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0894, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0894 BINDING SITE1 and KIAA0894 BINDING SITE2, designated SEQ ID:17059 and SEQ ID:17060 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64947] Another function of VGAM1929 is therefore inhibition of KIAA0894 (Accession NM\_014896). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with KIAA0894. KIAA0931 (Accession XM\_041191) is another VGAM1929 host target gene. KIAA0931 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0931, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0931 BINDING SITE, designated SEQ ID:33489, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64948] Another function of VGAM1929 is therefore inhibition of KIAA0931 (Accession XM\_041191). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0931. KIAA1033 (Accession XM\_035313) is another VGAM1929 host target gene. KIAA1033 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1033, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1033 BINDING SITE, designated SEQ ID:32230, to the

nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64949] Another function of VGAM1929 is therefore inhibition of KIAA1033 (Accession XM\_035313). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1033. KIAA1034 (Accession XM\_031223) is another VGAM1929 host target gene. KIAA1034 BINDING SITE1 and KIAA1034 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1034, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1034 BINDING SITE1 and KIAA1034 BINDING SITE2, designated SEQ ID:31309 and SEQ ID:31312 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64950] Another function of VGAM1929 is therefore inhibition of KIAA1034 (Accession XM\_031223). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1034. KIAA1040 (Accession XM\_051091) is another

VGAM1929 host target gene. KIAA1040 BINDING SITE1 and KIAA1040 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1040, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1040 BINDING SITE1 and KIAA1040 BINDING SITE2, designated SEQ ID:35747 and SEQ ID:33954 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64951] Another function of VGAM1929 is therefore inhibition of KIAA1040 (Accession XM\_051091). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1040. KIAA1164 (Accession XM\_045358) is another VGAM1929 host target gene. KIAA1164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1164 BINDING SITE, designated SEQ ID:34443, to the

nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64952] Another function of VGAM1929 is therefore inhibition of KIAA1164 (Accession XM\_045358). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1164. KIAA1190 (Accession XM\_048695) is another VGAM1929 host target gene. KIAA1190 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1190 BINDING SITE, designated SEQ ID:35227, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64953] Another function of VGAM1929 is therefore inhibition of KIAA1190 (Accession XM\_048695). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1190. KIAA1200 (Accession XM\_031054) is another VGAM1929 host target gene. KIAA1200 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1200, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1200 BINDING SITE, designated SEQ ID:31263, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64954] Another function of VGAM1929 is therefore inhibition of KIAA1200 (Accession XM\_031054). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1200. KIAA1223 (Accession XM\_048747) is another VGAM1929 host target gene. KIAA1223 BINDING SITE1 and KIAA1223 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1223, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1223 BINDING SITE1 and KIAA1223 BINDING SITE2, designated SEQ ID:35248 and SEQ ID:35251 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64955] Another function of VGAM1929 is therefore inhibition of KIAA1223 (Accession XM\_048747). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1223. KIAA1280 (Accession XM\_045766) is another VGAM1929 host target gene. KIAA1280 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1280 BINDING SITE, designated SEQ ID:34552, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64956] Another function of VGAM1929 is therefore inhibition of KIAA1280 (Accession XM\_045766). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1280. KIAA1297 (Accession XM\_051005) is another VGAM1929 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35721, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64957] Another function of VGAM1929 is therefore inhibition of KIAA1297 (Accession XM\_051005). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. KIAA1318 (Accession XM\_041080) is another VGAM1929 host target gene. KIAA1318 BINDING SITE1 and KIAA1318 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1318, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1318 BINDING SITE1 and KIAA1318 BINDING SITE2, designated SEQ ID:33430 and SEQ ID:33431 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64958] Another function of VGAM1929 is therefore inhibition of KIAA1318 (Accession XM\_041080). Accordingly, utilities

of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1318. KIAA1434 (Accession XM\_045585) is another VGAM1929 host target gene. KIAA1434 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1434 BINDING SITE, designated SEQ ID:34490, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64959] Another function of VGAM1929 is therefore inhibition of KIAA1434 (Accession XM\_045585). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1434. KIAA1437 (Accession XM\_026998) is another VGAM1929 host target gene. KIAA1437 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of



KIAA1437 BINDING SITE, designated SEQ ID:30385, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64960] Another function of VGAM1929 is therefore inhibition of KIAA1437 (Accession XM\_026998). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1437. KIAA1492 (Accession XM\_035312) is another VGAM1929 host target gene. KIAA1492 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1492, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1492 BINDING SITE, designated SEQ ID:32227, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64961] Another function of VGAM1929 is therefore inhibition of KIAA1492 (Accession XM\_035312). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1492. KIAA1495 (Accession XM\_055080) is another VGAM1929 host target gene. KIAA1495 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1495 BINDING SITE, designated SEQ ID:36227, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64962] Another function of VGAM1929 is therefore inhibition of KIAA1495 (Accession XM\_055080). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1495. KIAA1509 (Accession XM\_029353) is another VGAM1929 host target gene. KIAA1509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1509 BINDING SITE, designated SEQ ID:30878, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64963] Another function of VGAM1929 is therefore inhibition of

KIAA1509 (Accession XM\_029353). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1509. KIAA1511 (Accession XM\_046581) is another VGAM1929 host target gene. KIAA1511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1511 BINDING SITE, designated SEQ ID:34757, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64964] Another function of VGAM1929 is therefore inhibition of KIAA1511 (Accession XM\_046581). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1511. KIAA1530 (Accession XM\_042661) is another VGAM1929 host target gene. KIAA1530 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1530, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1530 BINDING SITE, designated SEQ ID:33732, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64965] Another function of VGAM1929 is therefore inhibition of KIAA1530 (Accession XM\_042661). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1530. KIAA1559 (Accession XM\_054472) is another VGAM1929 host target gene. KIAA1559 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1559 BINDING SITE, designated SEQ ID:36162, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64966] Another function of VGAM1929 is therefore inhibition of KIAA1559 (Accession XM\_054472). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1559. KIAA1577 (Accession XM\_035299) is another

VGAM1929 host target gene. KIAA1577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1577 BINDING SITE, designated SEQ ID:32211, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64967] Another function of VGAM1929 is therefore inhibition of KIAA1577 (Accession XM\_035299). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1577. KIAA1677 (Accession XM\_040383) is another VGAM1929 host target gene. KIAA1677 BINDING SITE1 and KIAA1677 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1677, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1677 BINDING SITE1 and KIAA1677 BINDING SITE2, designated SEQ ID:33291 and SEQ ID:33294 respectively, to the nucleotide sequence of

VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64968] Another function of VGAM1929 is therefore inhibition of KIAA1677 (Accession XM\_040383). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1677. KIAA1826 (Accession XM\_040784) is another VGAM1929 host target gene. KIAA1826 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1826 BINDING SITE, designated SEQ ID:33379, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64969] Another function of VGAM1929 is therefore inhibition of KIAA1826 (Accession XM\_040784). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1826. KIAA1831 (Accession XM\_033366) is another VGAM1929 host target gene. KIAA1831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1831 BINDING SITE, designated SEQ ID:31903, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64970] Another function of VGAM1929 is therefore inhibition of KIAA1831 (Accession XM\_033366). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1831. KIAA1878 (Accession XM\_166256) is another VGAM1929 host target gene. KIAA1878 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1878, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1878 BINDING SITE, designated SEQ ID:44076, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64971] Another function of VGAM1929 is therefore inhibition of KIAA1878 (Accession XM\_166256). Accordingly, utilities

of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1878. KIAA1987 (Accession XM\_113870) is another VGAM1929 host target gene. KIAA1987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1987 BINDING SITE, designated SEQ ID:42496, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64972] Another function of VGAM1929 is therefore inhibition of KIAA1987 (Accession XM\_113870). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1987. Karyopherin (importin) Beta 3 (KPNB3, Accession NM\_002271) is another VGAM1929 host target gene. KPNB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KPNB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-



quences of KPNB3 BINDING SITE, designated SEQ ID:8064, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64973] Another function of VGAM1929 is therefore inhibition of Karyopherin (importin) Beta 3 (KPNB3, Accession NM\_002271). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KPNB3. Leptin Receptor Overlapping Transcript-like 1 (LEPROTL1, Accession NM\_015344) is another VGAM1929 host target gene. LEPROTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEPROTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEPROTL1 BINDING SITE, designated SEQ ID:17651, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64974] Another function of VGAM1929 is therefore inhibition of Leptin Receptor Overlapping Transcript-like 1 (LEPROTL1, Accession NM\_015344). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LEP-ROTL1. LIG-1 (Accession XM\_033712) is another VGAM1929 host target gene. LIG-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIG-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIG-1 BINDING SITE, designated SEQ ID:31955, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64975] Another function of VGAM1929 is therefore inhibition of LIG-1 (Accession XM\_033712). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIG-1. Low Density Lipoprotein-related Protein 1B (deleted in tumors) (LRP1B, Accession NM\_018557) is another VGAM1929 host target gene. LRP1B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LRP1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP1B BINDING SITE,

designated SEQ ID:20638, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64976] Another function of VGAM1929 is therefore inhibition of Low Density Lipoprotein-related Protein 1B (deleted in tumors) (LRP1B, Accession NM\_018557). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP1B. Leucine Rich Repeat (in FLII) Interacting Protein 2 (LRRFIP2, Accession NM\_017724) is another VGAM1929 host target gene. LRRFIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRRFIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRRFIP2 BINDING SITE, designated SEQ ID:19313, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64977] Another function of VGAM1929 is therefore inhibition of Leucine Rich Repeat (in FLII) Interacting Protein 2 (LRRFIP2, Accession NM\_017724). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LR-RFIP2. Microtubule-actin Crosslinking Factor 1 (MACF1, Accession NM\_012090) is another VGAM1929 host target gene. MACF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MACF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MACF1 BINDING SITE, designated SEQ ID:14377, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64978] Another function of VGAM1929 is therefore inhibition of Microtubule-actin Crosslinking Factor 1 (MACF1, Accession NM\_012090). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MACF1. Mitogen-activated Protein Kinase Kinase Kinase Kinase 3 (MAP4K3, Accession NM\_003618) is another VGAM1929 host target gene. MAP4K3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP4K3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of MAP4K3 BINDING SITE, designated SEQ ID:9681, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64979] Another function of VGAM1929 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 3 (MAP4K3, Accession NM\_003618). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP4K3. Methionine Adenosyltransferase II, Beta (MAT2B, Accession NM\_013283) is another VGAM1929 host target gene. MAT2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAT2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAT2B BINDING SITE, designated SEQ ID:14955, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64980] Another function of VGAM1929 is therefore inhibition of Methionine Adenosyltransferase II, Beta (MAT2B, Acces-

sion NM\_013283). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAT2B. MCM10 Minichromosome Maintenance Deficient 10 (*S. cerevisiae*) (MCM10, Accession NM\_018518) is another VGAM1929 host target gene. MCM10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MCM10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCM10 BINDING SITE, designated SEQ ID:20593, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64981] Another function of VGAM1929 is therefore inhibition of MCM10 Minichromosome Maintenance Deficient 10 (*S. cerevisiae*) (MCM10, Accession NM\_018518). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCM10. MGC1203 (Accession NM\_024296) is another VGAM1929 host target gene. MGC1203 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC1203, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC1203 BINDING SITE, designated SEQ ID:23576, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64982] Another function of VGAM1929 is therefore inhibition of MGC1203 (Accession NM\_024296). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC1203. MGC13090 (Accession NM\_032711) is another VGAM1929 host target gene. MGC13090 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13090, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13090 BINDING SITE, designated SEQ ID:26426, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64983] Another function of VGAM1929 is therefore inhibition of MGC13090 (Accession NM\_032711). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC13090. MGC16075 (Accession NM\_032761) is another VGAM1929 host target gene. MGC16075 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16075, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16075 BINDING SITE, designated SEQ ID:26504, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64984] Another function of VGAM1929 is therefore inhibition of MGC16075 (Accession NM\_032761). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16075. MGC2474 (Accession NM\_023931) is another VGAM1929 host target gene. MGC2474 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2474, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2474 BINDING SITE, designated SEQ ID:23418, to the nucleotide



sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64985] Another function of VGAM1929 is therefore inhibition of MGC2474 (Accession NM\_023931). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2474. MGC3329 (Accession NM\_024086) is another VGAM1929 host target gene. MGC3329 BINDING SITE1 and MGC3329 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MGC3329, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3329 BINDING SITE1 and MGC3329 BINDING SITE2, designated SEQ ID:23527 and SEQ ID:23529 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64986] Another function of VGAM1929 is therefore inhibition of MGC3329 (Accession NM\_024086). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3329. MGC5508 (Accession NM\_024092) is another

VGAM1929 host target gene. MGC5508 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC5508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5508 BINDING SITE, designated SEQ ID:23535, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64987] Another function of VGAM1929 is therefore inhibition of MGC5508 (Accession NM\_024092). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5508. Myeloid/lymphoid Or Mixed-lineage Leukemia3 (MLL3, Accession NM\_021230) is another VGAM1929 host target gene. MLL3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MLL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLL3 BINDING SITE, designated SEQ ID:22202, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4640.

[64988] Another function of VGAM1929 is therefore inhibition of Myeloid/lymphoid Or Mixed-lineage Leukemia3 (MLL3, Accession NM\_021230). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLL3. N-acetylated Alpha-linked Acidic Dipeptidase 2 (NAALAD2, Accession NM\_005467) is another VGAM1929 host target gene. NAALAD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAALAD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAALAD2 BINDING SITE, designated SEQ ID:11964, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64989] Another function of VGAM1929 is therefore inhibition of N-acetylated Alpha-linked Acidic Dipeptidase 2 (NAALAD2, Accession NM\_005467). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAALAD2. NFASC (Accession XM\_046808) is another

VGAM1929 host target gene. NFASC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFASC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFASC BINDING SITE, designated SEQ ID:34830, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64990] Another function of VGAM1929 is therefore inhibition of NFASC (Accession XM\_046808). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFASC. NIBAN (Accession NM\_022083) is another VGAM1929 host target gene. NIBAN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NIBAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIBAN BINDING SITE, designated SEQ ID:22629, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64991] Another function of VGAM1929 is therefore inhibition of NIBAN (Accession NM\_022083). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIBAN. Nicolin 1 (NICN1, Accession NM\_032316) is another VGAM1929 host target gene. NICN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NICN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NICN1 BINDING SITE, designated SEQ ID:26117, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64992] Another function of VGAM1929 is therefore inhibition of Nicolin 1 (NICN1, Accession NM\_032316). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NICN1. NKX2B (Accession NM\_002509) is another VGAM1929 host target gene. NKX2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NKX2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NKX2B BINDING SITE, designated SEQ ID:8344, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64993] Another function of VGAM1929 is therefore inhibition of NKX2B (Accession NM\_002509). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NKX2B. NRF (Accession NM\_017544) is another VGAM1929 host target gene. NRF BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRF BINDING SITE, designated SEQ ID:18989, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64994] Another function of VGAM1929 is therefore inhibition of NRF (Accession NM\_017544). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRF.

NY-REN-25 (Accession XM\_027116) is another VGAM1929 host target gene. NY-REN-25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NY-REN-25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-25 BINDING SITE, designated SEQ ID:30416, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64995] Another function of VGAM1929 is therefore inhibition of NY-REN-25 (Accession XM\_027116). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-25. NY-REN-41 (Accession NM\_080654) is another VGAM1929 host target gene. NY-REN-41 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NY-REN-41, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-41 BINDING SITE, designated SEQ ID:27942, to the nucleotide sequence of VGAM1929 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4640.

[64996] Another function of VGAM1929 is therefore inhibition of NY-REN-41 (Accession NM\_080654). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-41. Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM\_015550) is another VGAM1929 host target gene. OSBPL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL3 BINDING SITE, designated SEQ ID:17821, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64997] Another function of VGAM1929 is therefore inhibition of Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM\_015550). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL3. P450RAI-2 (Accession NM\_019885) is another VGAM1929 host target gene. P450RAI-2 BINDING SITE is HOST TARGET binding



site found in the 3` untranslated region of mRNA encoded by P450RAI-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P450RAI-2 BINDING SITE, designated SEQ ID:21272, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64998] Another function of VGAM1929 is therefore inhibition of P450RAI-2 (Accession NM\_019885). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P450RAI-2. poly(A) Binding Protein, Cytoplasmic 5 (PABPC5, Accession NM\_080832) is another VGAM1929 host target gene. PABPC5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PABPC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PABPC5 BINDING SITE, designated SEQ ID:28096, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[64999] Another function of VGAM1929 is therefore inhibition of poly(A) Binding Protein, Cytoplasmic 5 (PABPC5, Accession NM\_080832). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PABPC5. PC4 (Accession NM\_006713) is another VGAM1929 host target gene. PC4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PC4 BINDING SITE, designated SEQ ID:13541, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65000] Another function of VGAM1929 is therefore inhibition of PC4 (Accession NM\_006713). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PC4. Protocadherin 19 (PCDH19, Accession XM\_033173) is another VGAM1929 host target gene. PCDH19 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PCDH19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH19 BINDING SITE, designated SEQ ID:31864, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65001] Another function of VGAM1929 is therefore inhibition of Protocadherin 19 (PCDH19, Accession XM\_033173). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH19. Period Homolog 3 (Drosophila) (PER3, Accession NM\_016831) is another VGAM1929 host target gene. PER3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER3 BINDING SITE, designated SEQ ID:18823, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65002] Another function of VGAM1929 is therefore inhibition of Period Homolog 3 (Drosophila) (PER3, Accession NM\_016831). Accordingly, utilities of VGAM1929 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with PER3. Phytoceramidase, Alkaline (PHCA, Accession NM\_018367) is another VGAM1929 host target gene. PHCA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHCA BINDING SITE, designated SEQ ID:20379, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65003] Another function of VGAM1929 is therefore inhibition of Phytoceramidase, Alkaline (PHCA, Accession NM\_018367). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHCA. PHRET1 (Accession NM\_021200) is another VGAM1929 host target gene. PHRET1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHRET1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of PHRET1 BINDING SITE, designated SEQ ID:22177, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65004] Another function of VGAM1929 is therefore inhibition of PHRET1 (Accession NM\_021200). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHRET1. Protease Inhibitor 15 (PI15, Accession NM\_015886) is another VGAM1929 host target gene. PI15 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PI15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PI15 BINDING SITE, designated SEQ ID:18030, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65005] Another function of VGAM1929 is therefore inhibition of Protease Inhibitor 15 (PI15, Accession NM\_015886). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PI15. Phosphatidylinositol-4-phosphate

5-kinase, Type II, Beta (PIP5K2B, Accession NM\_003559) is another VGAM1929 host target gene. PIP5K2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP5K2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP5K2B BINDING SITE, designated SEQ ID:9610, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65006] Another function of VGAM1929 is therefore inhibition of Phosphatidylinositol-4-phosphate 5-kinase, Type II, Beta (PIP5K2B, Accession NM\_003559). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP5K2B. PLPL (Accession NM\_020181) is another VGAM1929 host target gene. PLPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLPL BINDING SITE, designated SEQ ID:21399, to the nucleotide sequence of

VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65007] Another function of VGAM1929 is therefore inhibition of PLPL (Accession NM\_020181). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLPL. Paired Mesoderm Homeobox 2b (PMX2B, Accession NM\_003924) is another VGAM1929 host target gene. PMX2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMX2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMX2B BINDING SITE, designated SEQ ID:10016, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65008] Another function of VGAM1929 is therefore inhibition of Paired Mesoderm Homeobox 2b (PMX2B, Accession NM\_003924). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMX2B. Protein O-fucosyltransferase 1 (POFUT1, Accession XM\_047011) is

another VGAM1929 host target gene. POFUT1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by POFUT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POFUT1 BINDING SITE, designated SEQ ID:34885, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65009] Another function of VGAM1929 is therefore inhibition of Protein O-fucosyltransferase 1 (POFUT1, Accession XM\_047011). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POFUT1. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 1B (dopamine and cAMP regulated phosphoprotein, DARPP-32) (PPP1R1B, Accession NM\_032192) is another VGAM1929 host target gene. PPP1R1B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPP1R1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R1B BINDING SITE,



designated SEQ ID:25907, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65010] Another function of VGAM1929 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 1B (dopamine and cAMP regulated phosphoprotein, DARPP-32) (PPP1R1B, Accession NM\_032192). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R1B. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM\_024607) is another VGAM1929 host target gene. PPP1R3B BINDING SITE1 and PPP1R3B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PPP1R3B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R3B BINDING SITE1 and PPP1R3B BINDING SITE2, designated SEQ ID:23861 and SEQ ID:23862 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65011] Another function of VGAM1929 is therefore inhibition of

Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM\_024607). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R3B. Preimplantation Protein 3 (PREI3, Accession XM\_038960) is another VGAM1929 host target gene. PREI3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PREI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PREI3 BINDING SITE, designated SEQ ID:32964, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65012] Another function of VGAM1929 is therefore inhibition of Preimplantation Protein 3 (PREI3, Accession XM\_038960). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PREI3. PRMT3 (Accession XM\_036392) is another VGAM1929 host target gene. PRMT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRMT3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRMT3 BINDING SITE, designated SEQ ID:32437, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65013] Another function of VGAM1929 is therefore inhibition of PRMT3 (Accession XM\_036392). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRMT3. PRMT6 (Accession NM\_018137) is another VGAM1929 host target gene. PRMT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRMT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRMT6 BINDING SITE, designated SEQ ID:19934, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65014] Another function of VGAM1929 is therefore inhibition of PRMT6 (Accession NM\_018137). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PRMT6. PRO0246 (Accession NM\_014123) is another VGAM1929 host target gene. PRO0246 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0246, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0246 BINDING SITE, designated SEQ ID:15381, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65015] Another function of VGAM1929 is therefore inhibition of PRO0246 (Accession NM\_014123). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0246. PRO0767 (Accession NM\_014083) is another VGAM1929 host target gene. PRO0767 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0767, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0767 BINDING SITE, designated SEQ ID:15310, to the nucleotide

sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65016] Another function of VGAM1929 is therefore inhibition of PRO0767 (Accession NM\_014083). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0767. Protein Tyrosine Phosphatase Type IVA, Member 1 (PTP4A1, Accession NM\_003463) is another VGAM1929 host target gene. PTP4A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTP4A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTP4A1 BINDING SITE, designated SEQ ID:9533, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65017] Another function of VGAM1929 is therefore inhibition of Protein Tyrosine Phosphatase Type IVA, Member 1 (PTP4A1, Accession NM\_003463). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTP4A1. Rab11-FIP2 (Accession NM\_014904) is another

VGAM1929 host target gene. Rab11-FIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Rab11-FIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rab11-FIP2 BINDING SITE, designated SEQ ID:17101, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65018] Another function of VGAM1929 is therefore inhibition of Rab11-FIP2 (Accession NM\_014904). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rab11-FIP2. RAB3GAP (Accession XM\_040048) is another VGAM1929 host target gene. RAB3GAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB3GAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB3GAP BINDING SITE, designated SEQ ID:33246, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65019] Another function of VGAM1929 is therefore inhibition of RAB3GAP (Accession XM\_040048). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB3GAP. RAI (Accession NM\_006663) is another VGAM1929 host target gene. RAI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI BINDING SITE, designated SEQ ID:13474, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65020] Another function of VGAM1929 is therefore inhibition of RAI (Accession NM\_006663). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI. Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM\_014737) is another VGAM1929 host target gene. RASSF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASSF2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASSF2 BINDING SITE, designated SEQ ID:16401, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65021] Another function of VGAM1929 is therefore inhibition of Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM\_014737). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASSF2. RAS-like, Estrogen-regulated, Growth-inhibitor (RERG, Accession NM\_032918) is another VGAM1929 host target gene. RERG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RERG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RERG BINDING SITE, designated SEQ ID:26740, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65022] Another function of VGAM1929 is therefore inhibition of



RAS-like, Estrogen-regulated, Growth-inhibitor (RERG, Accession NM\_032918). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RERG. Rho-related BTB Domain Containing 3 (RHOBTB3, Accession NM\_014899) is another VGAM1929 host target gene. RHOBTB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RHOBTB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHOBTB3 BINDING SITE, designated SEQ ID:17079, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65023] Another function of VGAM1929 is therefore inhibition of Rho-related BTB Domain Containing 3 (RHOBTB3, Accession NM\_014899). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHOBTB3. RI58 (Accession NM\_012420) is another VGAM1929 host target gene. RI58 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

RI58, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RI58 BINDING SITE, designated SEQ ID:14796, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65024] Another function of VGAM1929 is therefore inhibition of RI58 (Accession NM\_012420). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RI58. RNAHP (Accession NM\_007372) is another VGAM1929 host target gene. RNAHP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNAHP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNAHP BINDING SITE, designated SEQ ID:14302, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65025] Another function of VGAM1929 is therefore inhibition of RNAHP (Accession NM\_007372). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with RNAHP. Ring Finger Protein 2 (RNF2, Accession NM\_007212) is another VGAM1929 host target gene. RNF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF2 BINDING SITE, designated SEQ ID:14075, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65026] Another function of VGAM1929 is therefore inhibition of Ring Finger Protein 2 (RNF2, Accession NM\_007212). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF2. RNA Binding Protein S1, Serine-rich Domain (RNPS1, Accession NM\_006711) is another VGAM1929 host target gene. RNPS1 BINDING SITE1 and RNPS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RNPS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of RNPS1 BINDING SITE1 and RNPS1 BINDING SITE2, designated SEQ ID:13539 and SEQ ID:27904 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65027] Another function of VGAM1929 is therefore inhibition of RNA Binding Protein S1, Serine-rich Domain (RNPS1, Accession NM\_006711). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNPS1. SCAN Domain Containing 2 (SCAND2, Accession NM\_022050) is another VGAM1929 host target gene. SCAND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCAND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAND2 BINDING SITE, designated SEQ ID:22575, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65028] Another function of VGAM1929 is therefore inhibition of SCAN Domain Containing 2 (SCAND2, Accession NM\_022050). Accordingly, utilities of VGAM1929 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with SCAND2. SEC63L (Accession NM\_007214) is another VGAM1929 host target gene. SEC63L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC63L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC63L BINDING SITE, designated SEQ ID:14080, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65029] Another function of VGAM1929 is therefore inhibition of SEC63L (Accession NM\_007214). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC63L. SH3 Domain Binding Glutamic Acid-rich Protein Like (SH3BGRL, Accession XM\_030373) is another VGAM1929 host target gene. SH3BGRL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of SH3BGRL BINDING SITE, designated SEQ ID:31024, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65030] Another function of VGAM1929 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like (SH3BGRL, Accession XM\_030373). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BGRL. SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM\_031469) is another VGAM1929 host target gene. SH3BGRL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL2 BINDING SITE, designated SEQ ID:25530, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65031] Another function of VGAM1929 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM\_031469). Accordingly, utilities

of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BGRL2. Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM\_000617) is another VGAM1929 host target gene. SLC11A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC11A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC11A2 BINDING SITE, designated SEQ ID:6224, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65032] Another function of VGAM1929 is therefore inhibition of Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM\_000617). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC11A2. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM\_018450) is another VGAM1929 host target gene.

SMARCF1 BINDING SITE1 through SMARCF1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMARCF1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCF1 BINDING SITE1 through SMARCF1 BINDING SITE3, designated SEQ ID:20519, SEQ ID:29162 and SEQ ID:12624 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65033] Another function of VGAM1929 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM\_018450). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCF1. Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM\_004863) is another VGAM1929 host target gene. SPTLC2 BINDING SITE1 and SPTLC2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SPTLC2, corresponding to HOST TARGET binding sites



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTLC2 BINDING SITE1 and SPTLC2 BINDING SITE2, designated SEQ ID:11279 and SEQ ID:11280 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65034] Another function of VGAM1929 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM\_004863). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. Suppression of Tumorigenicity 13 (colon carcinoma) (Hsp70 interacting protein) (ST13, Accession NM\_003932) is another VGAM1929 host target gene. ST13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ST13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST13 BINDING SITE, designated SEQ ID:10035, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65035] Another function of VGAM1929 is therefore inhibition of Suppression of Tumorigenicity 13 (colon carcinoma) (Hsp70 interacting protein) (ST13, Accession NM\_003932). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST13. Suppression of Tumorigenicity 7 Like (ST7L, Accession NM\_017744) is another VGAM1929 host target gene. ST7L BINDING SITE1 through ST7L BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ST7L, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST7L BINDING SITE1 through ST7L BINDING SITE3, designated SEQ ID:19338, SEQ ID:29211 and SEQ ID:28980 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65036] Another function of VGAM1929 is therefore inhibition of Suppression of Tumorigenicity 7 Like (ST7L, Accession NM\_017744). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST7L. Signal Transducer

and Activator of Transcription 5A (STAT5A, Accession NM\_003152) is another VGAM1929 host target gene. STAT5A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAT5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAT5A BINDING SITE, designated SEQ ID:9128, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65037] Another function of VGAM1929 is therefore inhibition of Signal Transducer and Activator of Transcription 5A (STAT5A, Accession NM\_003152). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAT5A. Serine/threonine Kinase 36 (fused homolog, Drosophila) (STK36, Accession XM\_050803) is another VGAM1929 host target gene. STK36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of STK36 BINDING SITE, designated SEQ ID:35691, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65038] Another function of VGAM1929 is therefore inhibition of Serine/threonine Kinase 36 (fused homolog, Drosophila) (STK36, Accession XM\_050803). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK36. STRIN (Accession NM\_016271) is another VGAM1929 host target gene. STRIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STRIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRIN BINDING SITE, designated SEQ ID:18395, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65039] Another function of VGAM1929 is therefore inhibition of STRIN (Accession NM\_016271). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRIN.

Striatin, Calmodulin Binding Protein 3 (STRN3, Accession NM\_014574) is another VGAM1929 host target gene. STRN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STRN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRN3 BINDING SITE, designated SEQ ID:15936, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65040] Another function of VGAM1929 is therefore inhibition of Striatin, Calmodulin Binding Protein 3 (STRN3, Accession NM\_014574). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRN3. Synaptophysin-like Protein (SYPL, Accession XM\_167511) is another VGAM1929 host target gene. SYPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYPL BINDING SITE, desig-

nated SEQ ID:44646, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65041] Another function of VGAM1929 is therefore inhibition of Synaptophysin-like Protein (SYPL, Accession XM\_167511). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYPL. Synaptotagmin-like 2 (SYTL2, Accession NM\_032943) is another VGAM1929 host target gene. SYTL2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SYTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYTL2 BINDING SITE, designated SEQ ID:26760, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65042] Another function of VGAM1929 is therefore inhibition of Synaptotagmin-like 2 (SYTL2, Accession NM\_032943). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYTL2. TA-PP2C (Accession NM\_139283)

is another VGAM1929 host target gene. TA-PP2C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TA-PP2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TA-PP2C BINDING SITE, designated SEQ ID:29286, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65043] Another function of VGAM1929 is therefore inhibition of TA-PP2C (Accession NM\_139283). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TA-PP2C. TAF5-like RNA Polymerase II, P300/CBP-associated Factor (PCAF)-associated Factor, 65kDa (TAF5L, Accession NM\_014409) is another VGAM1929 host target gene. TAF5L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAF5L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF5L BINDING SITE, designated SEQ ID:15750, to the nucleotide sequence of VGAM1929 RNA,

herein designated VGAM RNA, also designated SEQ ID:4640.

[65044] Another function of VGAM1929 is therefore inhibition of TAF5-like RNA Polymerase II, P300/CBP-associated Factor (PCAF)-associated Factor, 65kDa (TAF5L, Accession NM\_014409). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF5L. TAF9-like RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 31kDa (TAF9L, Accession NM\_015975) is another VGAM1929 host target gene. TAF9L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAF9L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF9L BINDING SITE, designated SEQ ID:18076, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65045] Another function of VGAM1929 is therefore inhibition of TAF9-like RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 31kDa (TAF9L, Accession NM\_015975). Accordingly, utilities of VGAM1929 include



diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF9L. TBDN100 (Accession NM\_025085) is another VGAM1929 host target gene. TBDN100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBDN100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBDN100 BINDING SITE, designated SEQ ID:24695, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65046] Another function of VGAM1929 is therefore inhibition of TBDN100 (Accession NM\_025085). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBDN100. Transcription Factor-like 5 (basic helix-loop-helix) (TCFL5, Accession NM\_006602) is another VGAM1929 host target gene. TCFL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of TCFL5 BINDING SITE, designated SEQ ID:13382, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65047] Another function of VGAM1929 is therefore inhibition of Transcription Factor-like 5 (basic helix-loop-helix) (TCFL5, Accession NM\_006602). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCFL5. T-cell Leukemia/lymphoma 6 (TCL6, Accession NM\_012468) is another VGAM1929 host target gene. TCL6 BINDING SITE1 through TCL6 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCL6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCL6 BINDING SITE1 through TCL6 BINDING SITE4, designated SEQ ID:14846, SEQ ID:15770, SEQ ID:21772 and SEQ ID:21763 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65048] Another function of VGAM1929 is therefore inhibition of

T-cell Leukemia/lymphoma 6 (TCL6, Accession NM\_012468). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCL6. TIP-1 (Accession NM\_014604) is another VGAM1929 host target gene. TIP-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIP-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIP-1 BINDING SITE, designated SEQ ID:15966, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65049] Another function of VGAM1929 is therefore inhibition of TIP-1 (Accession NM\_014604). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIP-1. Trinucleotide Repeat Containing 5 (TNRC5, Accession NM\_006586) is another VGAM1929 host target gene. TNRC5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TNRC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of TNRC5 BINDING SITE, designated SEQ ID:13346, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65050] Another function of VGAM1929 is therefore inhibition of Trinucleotide Repeat Containing 5 (TNRC5, Accession NM\_006586). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNRC5. Transducer of ERBB2, 2 (TOB2, Accession XM\_170995) is another VGAM1929 host target gene. TOB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOB2 BINDING SITE, designated SEQ ID:45768, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65051] Another function of VGAM1929 is therefore inhibition of Transducer of ERBB2, 2 (TOB2, Accession XM\_170995). Accordingly, utilities of VGAM1929 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with TOB2. TOLLIP (Accession NM\_019009) is another VGAM1929 host target gene. TOLLIP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TOLLIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOLLIP BINDING SITE, designated SEQ ID:21093, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65052] Another function of VGAM1929 is therefore inhibition of TOLLIP (Accession NM\_019009). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOLLIP. TOPK (Accession NM\_018492) is another VGAM1929 host target gene. TOPK BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TOPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOPK BINDING SITE, designated SEQ

ID:20554, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65053] Another function of VGAM1929 is therefore inhibition of TOPK (Accession NM\_018492). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOPK. Testis-specific Transcript, Y-linked 9 (TTY9, Accession NM\_031927) is another VGAM1929 host target gene. TTY9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TTY9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTY9 BINDING SITE, designated SEQ ID:25679, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65054] Another function of VGAM1929 is therefore inhibition of Testis-specific Transcript, Y-linked 9 (TTY9, Accession NM\_031927). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTY9. Ubiquitin-conju-

gating Enzyme E2G 1 (UBC7 homolog, *C. elegans*) (UBE2G1, Accession NM\_003342) is another VGAM1929 host target gene. UBE2G1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2G1 BINDING SITE, designated SEQ ID:9349, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65055] Another function of VGAM1929 is therefore inhibition of Ubiquitin-conjugating Enzyme E2G 1 (UBC7 homolog, *C. elegans*) (UBE2G1, Accession NM\_003342). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2G1. Unc-5 Homolog D (*C. elegans*) (UNC5D, Accession NM\_080872) is another VGAM1929 host target gene. UNC5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UNC5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of UNC5D BINDING SITE, designated SEQ ID:28116, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65056] Another function of VGAM1929 is therefore inhibition of Unc-5 Homolog D (C. elegans) (UNC5D, Accession NM\_080872). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNC5D. Ubiquitin Specific Protease 15 (USP15, Accession NM\_006313) is another VGAM1929 host target gene. USP15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP15 BINDING SITE, designated SEQ ID:13007, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65057] Another function of VGAM1929 is therefore inhibition of Ubiquitin Specific Protease 15 (USP15, Accession NM\_006313). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical



cal conditions associated with USP15. Ubiquitin Specific Protease 25 (USP25, Accession NM\_013396) is another VGAM1929 host target gene. USP25 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by USP25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP25 BINDING SITE, designated SEQ ID:15049, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65058] Another function of VGAM1929 is therefore inhibition of Ubiquitin Specific Protease 25 (USP25, Accession NM\_013396). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP25. Ubiquitin Specific Protease 8 (USP8, Accession NM\_005154) is another VGAM1929 host target gene. USP8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by USP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP8 BINDING SITE,

designated SEQ ID:11630, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65059] Another function of VGAM1929 is therefore inhibition of Ubiquitin Specific Protease 8 (USP8, Accession NM\_005154). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP8. VEZATIN (Accession NM\_017599) is another VGAM1929 host target gene. VEZATIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VEZATIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VEZATIN BINDING SITE, designated SEQ ID:19073, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65060] Another function of VGAM1929 is therefore inhibition of VEZATIN (Accession NM\_017599). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VEZATIN. VMP1 (Accession NM\_030938) is another

VGAM1929 host target gene. VMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VMP1 BINDING SITE, designated SEQ ID:25208, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65061] Another function of VGAM1929 is therefore inhibition of VMP1 (Accession NM\_030938). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VMP1. X123 (Accession XM\_046023) is another VGAM1929 host target gene. X123 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by X123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of X123 BINDING SITE, designated SEQ ID:34649, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65062] Another function of VGAM1929 is therefore inhibition of X123 (Accession XM\_046023). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with X123. Yes-associated Protein 1, 65kDa (YAP1, Accession NM\_006106) is another VGAM1929 host target gene. YAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YAP1 BINDING SITE, designated SEQ ID:12753, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65063] Another function of VGAM1929 is therefore inhibition of Yes-associated Protein 1, 65kDa (YAP1, Accession NM\_006106). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YAP1. Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Theta Polypeptide (YWHAQ, Accession NM\_006826) is another VGAM1929 host target gene. YWHAQ BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by YWHAQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YWHAQ BINDING SITE, designated SEQ ID:13707, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65064] Another function of VGAM1929 is therefore inhibition of Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Theta Polypeptide (YWHAQ, Accession NM\_006826). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YWHAQ. Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM\_053023) is another VGAM1929 host target gene. ZFP91 BINDING SITE1 through ZFP91 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ZFP91, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP91 BINDING SITE1 through ZFP91 BINDING SITE3, designated SEQ

ID:27575, SEQ ID:27573 and SEQ ID:27574 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65065] Another function of VGAM1929 is therefore inhibition of Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM\_053023). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP91. Zinc Finger Protein 323 (ZNF323, Accession NM\_030899) is another VGAM1929 host target gene. ZNF323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF323 BINDING SITE, designated SEQ ID:25169, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65066] Another function of VGAM1929 is therefore inhibition of Zinc Finger Protein 323 (ZNF323, Accession NM\_030899). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF323. ZNF361 (Accession

NM\_018555) is another VGAM1929 host target gene. ZNF361 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF361 BINDING SITE, designated SEQ ID:20636, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65067] Another function of VGAM1929 is therefore inhibition of ZNF361 (Accession NM\_018555). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF361. Zinc Finger Protein 363 (ZNF363, Accession XM\_055989) is another VGAM1929 host target gene. ZNF363 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF363, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF363 BINDING SITE, designated SEQ ID:36358, to the nucleotide sequence of VGAM1929 RNA,

herein designated VGAM RNA, also designated SEQ ID:4640.

[65068] Another function of VGAM1929 is therefore inhibition of Zinc Finger Protein 363 (ZNF363, Accession XM\_055989). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF363. LOC112885 (Accession NM\_138415) is another VGAM1929 host target gene. LOC112885 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112885, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112885 BINDING SITE, designated SEQ ID:28786, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65069] Another function of VGAM1929 is therefore inhibition of LOC112885 (Accession NM\_138415). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112885. LOC115297 (Accession XM\_053313) is another VGAM1929 host target gene. LOC115297 BINDING



SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115297 BINDING SITE, designated SEQ ID:36070, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65070] Another function of VGAM1929 is therefore inhibition of LOC115297 (Accession XM\_053313). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115297. LOC120856 (Accession XM\_058509) is another VGAM1929 host target gene. LOC120856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120856 BINDING SITE, designated SEQ ID:36638, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65071] Another function of VGAM1929 is therefore inhibition of

LOC120856 (Accession XM\_058509). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120856. LOC121219 (Accession XM\_058544) is another VGAM1929 host target gene. LOC121219 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC121219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121219 BINDING SITE, designated SEQ ID:36650, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65072] Another function of VGAM1929 is therefore inhibition of LOC121219 (Accession XM\_058544). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121219. LOC121838 (Accession XM\_071772) is another VGAM1929 host target gene. LOC121838 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC121838, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC121838 BINDING SITE, designated SEQ ID:37420, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65073] Another function of VGAM1929 is therefore inhibition of LOC121838 (Accession XM\_071772). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121838. LOC123036 (Accession XM\_058676) is another VGAM1929 host target gene. LOC123036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC123036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123036 BINDING SITE, designated SEQ ID:36717, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65074] Another function of VGAM1929 is therefore inhibition of LOC123036 (Accession XM\_058676). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123036. LOC126526 (Accession XM\_059053) is an-

other VGAM1929 host target gene. LOC126526 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126526, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126526 BINDING SITE, designated SEQ ID:36847, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65075] Another function of VGAM1929 is therefore inhibition of LOC126526 (Accession XM\_059053). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126526. LOC126528 (Accession XM\_059052) is another VGAM1929 host target gene. LOC126528 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC126528, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126528 BINDING SITE, designated SEQ ID:36844, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65076] Another function of VGAM1929 is therefore inhibition of LOC126528 (Accession XM\_059052). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126528. LOC131000 (Accession XM\_067145) is another VGAM1929 host target gene. LOC131000 BINDING SITE1 and LOC131000 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC131000, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131000 BINDING SITE1 and LOC131000 BINDING SITE2, designated SEQ ID:37352 and SEQ ID:37351 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65077] Another function of VGAM1929 is therefore inhibition of LOC131000 (Accession XM\_067145). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131000. LOC132235 (Accession XM\_072302) is another VGAM1929 host target gene. LOC132235 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC132235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132235 BINDING SITE, designated SEQ ID:37482, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65078] Another function of VGAM1929 is therefore inhibition of LOC132235 (Accession XM\_072302). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132235. LOC135398 (Accession XM\_069333) is another VGAM1929 host target gene. LOC135398 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135398, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135398 BINDING SITE, designated SEQ ID:37388, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65079] Another function of VGAM1929 is therefore inhibition of LOC135398 (Accession XM\_069333). Accordingly, utilities

of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135398. LOC139673 (Accession XM\_071645) is another VGAM1929 host target gene. LOC139673 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC139673, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139673 BINDING SITE, designated SEQ ID:37404, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65080] Another function of VGAM1929 is therefore inhibition of LOC139673 (Accession XM\_071645). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139673. LOC143310 (Accession XM\_084485) is another VGAM1929 host target gene. LOC143310 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC143310 BINDING SITE, designated SEQ ID:37607, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65081] Another function of VGAM1929 is therefore inhibition of LOC143310 (Accession XM\_084485). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143310. LOC143888 (Accession XM\_084669) is another VGAM1929 host target gene. LOC143888 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143888, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143888 BINDING SITE, designated SEQ ID:37669, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65082] Another function of VGAM1929 is therefore inhibition of LOC143888 (Accession XM\_084669). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143888. LOC145786 (Accession XM\_096860) is another VGAM1929 host target gene. LOC145786 BINDING



SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145786 BINDING SITE, designated SEQ ID:40593, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65083] Another function of VGAM1929 is therefore inhibition of LOC145786 (Accession XM\_096860). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145786. LOC145845 (Accession XM\_096884) is another VGAM1929 host target gene. LOC145845 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145845, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145845 BINDING SITE, designated SEQ ID:40616, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65084] Another function of VGAM1929 is therefore inhibition of

LOC145845 (Accession XM\_096884). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145845. LOC146138 (Accession XM\_096938) is another VGAM1929 host target gene. LOC146138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146138 BINDING SITE, designated SEQ ID:40655, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65085] Another function of VGAM1929 is therefore inhibition of LOC146138 (Accession XM\_096938). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146138. LOC146515 (Accession XM\_085493) is another VGAM1929 host target gene. LOC146515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC146515 BINDING SITE, designated SEQ ID:38196, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65086] Another function of VGAM1929 is therefore inhibition of LOC146515 (Accession XM\_085493). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146515. LOC146713 (Accession XM\_097071) is another VGAM1929 host target gene. LOC146713 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146713 BINDING SITE, designated SEQ ID:40718, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65087] Another function of VGAM1929 is therefore inhibition of LOC146713 (Accession XM\_097071). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146713. LOC147136 (Accession XM\_085716) is an-

other VGAM1929 host target gene. LOC147136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147136 BINDING SITE, designated SEQ ID:38304, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65088] Another function of VGAM1929 is therefore inhibition of LOC147136 (Accession XM\_085716). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147136. LOC147353 (Accession XM\_097227) is another VGAM1929 host target gene. LOC147353 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147353, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147353 BINDING SITE, designated SEQ ID:40835, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65089] Another function of VGAM1929 is therefore inhibition of LOC147353 (Accession XM\_097227). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147353. LOC147515 (Accession XM\_097243) is another VGAM1929 host target gene. LOC147515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147515 BINDING SITE, designated SEQ ID:40843, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65090] Another function of VGAM1929 is therefore inhibition of LOC147515 (Accession XM\_097243). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147515. LOC147639 (Accession XM\_085822) is another VGAM1929 host target gene. LOC147639 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147639, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147639 BINDING SITE, designated SEQ ID:38345, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65091] Another function of VGAM1929 is therefore inhibition of LOC147639 (Accession XM\_085822). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147639. LOC148809 (Accession XM\_086325) is another VGAM1929 host target gene. LOC148809 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148809, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148809 BINDING SITE, designated SEQ ID:38595, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65092] Another function of VGAM1929 is therefore inhibition of LOC148809 (Accession XM\_086325). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC148809. LOC148936 (Accession XM\_097556) is another VGAM1929 host target gene. LOC148936 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148936 BINDING SITE, designated SEQ ID:40933, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65093] Another function of VGAM1929 is therefore inhibition of LOC148936 (Accession XM\_097556). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148936. LOC148938 (Accession XM\_097555) is another VGAM1929 host target gene. LOC148938 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148938, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148938 BINDING SITE, designated SEQ ID:40926, to the nucleotide sequence of VGAM1929 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4640.

[65094] Another function of VGAM1929 is therefore inhibition of LOC148938 (Accession XM\_097555). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148938. LOC149073 (Accession XM\_097577) is another VGAM1929 host target gene. LOC149073 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149073 BINDING SITE, designated SEQ ID:40944, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65095] Another function of VGAM1929 is therefore inhibition of LOC149073 (Accession XM\_097577). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149073. LOC149113 (Accession XM\_086425) is another VGAM1929 host target gene. LOC149113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149113, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149113 BINDING SITE, designated SEQ ID:38641, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65096] Another function of VGAM1929 is therefore inhibition of LOC149113 (Accession XM\_086425). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149113. LOC149267 (Accession NM\_138480) is another VGAM1929 host target gene. LOC149267 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149267 BINDING SITE, designated SEQ ID:28832, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65097] Another function of VGAM1929 is therefore inhibition of LOC149267 (Accession NM\_138480). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC149267. LOC149322 (Accession XM\_004762) is another VGAM1929 host target gene. LOC149322 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149322 BINDING SITE, designated SEQ ID:29946, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65098] Another function of VGAM1929 is therefore inhibition of LOC149322 (Accession XM\_004762). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149322. LOC149373 (Accession XM\_086507) is another VGAM1929 host target gene. LOC149373 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149373 BINDING SITE, designated SEQ ID:38722, to

the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65099] Another function of VGAM1929 is therefore inhibition of LOC149373 (Accession XM\_086507). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149373. LOC149670 (Accession XM\_086647) is another VGAM1929 host target gene. LOC149670 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149670, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149670 BINDING SITE, designated SEQ ID:38806, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65100] Another function of VGAM1929 is therefore inhibition of LOC149670 (Accession XM\_086647). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149670. LOC149692 (Accession XM\_097706) is another VGAM1929 host target gene. LOC149692 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC149692, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149692 BINDING SITE, designated SEQ ID:41040, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65101] Another function of VGAM1929 is therefore inhibition of LOC149692 (Accession XM\_097706). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149692. LOC149995 (Accession XM\_097798) is another VGAM1929 host target gene. LOC149995 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149995, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149995 BINDING SITE, designated SEQ ID:41128, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65102] Another function of VGAM1929 is therefore inhibition of LOC149995 (Accession XM\_097798). Accordingly, utilities

of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149995. LOC150142 (Accession XM\_086791) is another VGAM1929 host target gene. LOC150142 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150142 BINDING SITE, designated SEQ ID:38852, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65103] Another function of VGAM1929 is therefore inhibition of LOC150142 (Accession XM\_086791). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150142. LOC150271 (Accession XM\_097859) is another VGAM1929 host target gene. LOC150271 BINDING SITE1 and LOC150271 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC150271, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LOC150271 BINDING SITE1 and LOC150271 BINDING SITE2, designated SEQ ID:41168 and SEQ ID:41177 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65104] Another function of VGAM1929 is therefore inhibition of LOC150271 (Accession XM\_097859). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC150848 (Accession XM\_097959) is another VGAM1929 host target gene. LOC150848 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150848 BINDING SITE, designated SEQ ID:41263, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65105] Another function of VGAM1929 is therefore inhibition of LOC150848 (Accession XM\_097959). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC150848. LOC151277 (Accession XM\_087155) is another VGAM1929 host target gene. LOC151277 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151277 BINDING SITE, designated SEQ ID:39095, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65106] Another function of VGAM1929 is therefore inhibition of LOC151277 (Accession XM\_087155). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151277. LOC151361 (Accession XM\_098048) is another VGAM1929 host target gene. LOC151361 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151361 BINDING SITE, designated SEQ ID:41329, to the nucleotide sequence of VGAM1929 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4640.

[65107] Another function of VGAM1929 is therefore inhibition of LOC151361 (Accession XM\_098048). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151361. LOC151556 (Accession XM\_087239) is another VGAM1929 host target gene. LOC151556 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151556 BINDING SITE, designated SEQ ID:39132, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65108] Another function of VGAM1929 is therefore inhibition of LOC151556 (Accession XM\_087239). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151556. LOC151701 (Accession XM\_098109) is another VGAM1929 host target gene. LOC151701 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151701, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151701 BINDING SITE, designated SEQ ID:41387, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65109] Another function of VGAM1929 is therefore inhibition of LOC151701 (Accession XM\_098109). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151701. LOC151827 (Accession XM\_087317) is another VGAM1929 host target gene. LOC151827 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151827 BINDING SITE, designated SEQ ID:39169, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65110] Another function of VGAM1929 is therefore inhibition of LOC151827 (Accession XM\_087317). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC151827. LOC152559 (Accession XM\_087487) is another VGAM1929 host target gene. LOC152559 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152559 BINDING SITE, designated SEQ ID:39284, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65111] Another function of VGAM1929 is therefore inhibition of LOC152559 (Accession XM\_087487). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152559. LOC152804 (Accession XM\_098266) is another VGAM1929 host target gene. LOC152804 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152804, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152804 BINDING SITE, designated SEQ ID:41555, to

the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65112] Another function of VGAM1929 is therefore inhibition of LOC152804 (Accession XM\_098266). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152804. LOC153027 (Accession XM\_041221) is another VGAM1929 host target gene. LOC153027 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153027, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153027 BINDING SITE, designated SEQ ID:33491, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65113] Another function of VGAM1929 is therefore inhibition of LOC153027 (Accession XM\_041221). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153027. LOC153196 (Accession XM\_098323) is another VGAM1929 host target gene. LOC153196 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC153196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153196 BINDING SITE, designated SEQ ID:41596, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65114] Another function of VGAM1929 is therefore inhibition of LOC153196 (Accession XM\_098323). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153196. LOC153232 (Accession XM\_098331) is another VGAM1929 host target gene. LOC153232 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153232 BINDING SITE, designated SEQ ID:41598, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65115] Another function of VGAM1929 is therefore inhibition of LOC153232 (Accession XM\_098331). Accordingly, utilities

of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153232. LOC153346 (Accession XM\_098364) is another VGAM1929 host target gene. LOC153346 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153346 BINDING SITE, designated SEQ ID:41619, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65116] Another function of VGAM1929 is therefore inhibition of LOC153346 (Accession XM\_098364). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153346. LOC154043 (Accession XM\_087831) is another VGAM1929 host target gene. LOC154043 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC154043 BINDING SITE, designated SEQ ID:39461, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65117] Another function of VGAM1929 is therefore inhibition of LOC154043 (Accession XM\_087831). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154043. LOC154403 (Accession XM\_087919) is another VGAM1929 host target gene. LOC154403 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154403, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154403 BINDING SITE, designated SEQ ID:39469, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65118] Another function of VGAM1929 is therefore inhibition of LOC154403 (Accession XM\_087919). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154403. LOC154992 (Accession XM\_088106) is another VGAM1929 host target gene. LOC154992 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154992 BINDING SITE, designated SEQ ID:39519, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65119] Another function of VGAM1929 is therefore inhibition of LOC154992 (Accession XM\_088106). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154992. LOC155081 (Accession XM\_088145) is another VGAM1929 host target gene. LOC155081 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155081, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155081 BINDING SITE, designated SEQ ID:39545, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65120] Another function of VGAM1929 is therefore inhibition of

LOC155081 (Accession XM\_088145). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155081. LOC157503 (Accession XM\_098767) is another VGAM1929 host target gene. LOC157503 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157503, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157503 BINDING SITE, designated SEQ ID:41813, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65121] Another function of VGAM1929 is therefore inhibition of LOC157503 (Accession XM\_098767). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157503. LOC157653 (Accession XM\_088353) is another VGAM1929 host target gene. LOC157653 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157653, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC157653 BINDING SITE, designated SEQ ID:39635, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65122] Another function of VGAM1929 is therefore inhibition of LOC157653 (Accession XM\_088353). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157653. LOC158014 (Accession XM\_088442) is another VGAM1929 host target gene. LOC158014 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158014 BINDING SITE, designated SEQ ID:39692, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65123] Another function of VGAM1929 is therefore inhibition of LOC158014 (Accession XM\_088442). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158014. LOC158055 (Accession XM\_088453) is an-

other VGAM1929 host target gene. LOC158055 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158055, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158055 BINDING SITE, designated SEQ ID:39704, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65124] Another function of VGAM1929 is therefore inhibition of LOC158055 (Accession XM\_088453). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158055. LOC158382 (Accession XM\_098931) is another VGAM1929 host target gene. LOC158382 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158382 BINDING SITE, designated SEQ ID:41966, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65125] Another function of VGAM1929 is therefore inhibition of LOC158382 (Accession XM\_098931). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158382. LOC158549 (Accession XM\_098963) is another VGAM1929 host target gene. LOC158549 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158549 BINDING SITE, designated SEQ ID:42006, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65126] Another function of VGAM1929 is therefore inhibition of LOC158549 (Accession XM\_098963). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158549. LOC196027 (Accession XM\_113633) is another VGAM1929 host target gene. LOC196027 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196027, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196027 BINDING SITE, designated SEQ ID:42308, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65127] Another function of VGAM1929 is therefore inhibition of LOC196027 (Accession XM\_113633). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196027. LOC196446 (Accession XM\_113722) is another VGAM1929 host target gene. LOC196446 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196446, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196446 BINDING SITE, designated SEQ ID:42373, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65128] Another function of VGAM1929 is therefore inhibition of LOC196446 (Accession XM\_113722). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196446. LOC196761 (Accession XM\_116865) is another VGAM1929 host target gene. LOC196761 BINDING SITE1 and LOC196761 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC196761, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196761 BINDING SITE1 and LOC196761 BINDING SITE2, designated SEQ ID:43128 and SEQ ID:43130 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65129] Another function of VGAM1929 is therefore inhibition of LOC196761 (Accession XM\_116865). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196761. LOC197131 (Accession XM\_113823) is another VGAM1929 host target gene. LOC197131 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC197131 BINDING SITE, designated SEQ ID:42446, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65130] Another function of VGAM1929 is therefore inhibition of LOC197131 (Accession XM\_113823). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197131. LOC197319 (Accession XM\_113862) is another VGAM1929 host target gene. LOC197319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197319 BINDING SITE, designated SEQ ID:42478, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65131] Another function of VGAM1929 is therefore inhibition of LOC197319 (Accession XM\_113862). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197319. LOC199699 (Accession XM\_113990) is another VGAM1929 host target gene. LOC199699 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199699, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199699 BINDING SITE, designated SEQ ID:42595, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65132] Another function of VGAM1929 is therefore inhibition of LOC199699 (Accession XM\_113990). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199699. LOC199775 (Accession XM\_114016) is another VGAM1929 host target gene. LOC199775 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199775, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199775 BINDING SITE, designated SEQ ID:42616, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65133] Another function of VGAM1929 is therefore inhibition of

LOC199775 (Accession XM\_114016). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199775. LOC200014 (Accession XM\_114087) is another VGAM1929 host target gene. LOC200014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200014 BINDING SITE, designated SEQ ID:42697, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65134] Another function of VGAM1929 is therefore inhibition of LOC200014 (Accession XM\_114087). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200014. LOC200107 (Accession XM\_114121) is another VGAM1929 host target gene. LOC200107 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200107, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC200107 BINDING SITE, designated SEQ ID:42707, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65135] Another function of VGAM1929 is therefore inhibition of LOC200107 (Accession XM\_114121). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200107. LOC200138 (Accession XM\_117194) is another VGAM1929 host target gene. LOC200138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200138 BINDING SITE, designated SEQ ID:43281, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65136] Another function of VGAM1929 is therefore inhibition of LOC200138 (Accession XM\_117194). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200138. LOC200558 (Accession XM\_114258) is an-

other VGAM1929 host target gene. LOC200558 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200558 BINDING SITE, designated SEQ ID:42820, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65137] Another function of VGAM1929 is therefore inhibition of LOC200558 (Accession XM\_114258). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200558. LOC200563 (Accession XM\_117251) is another VGAM1929 host target gene. LOC200563 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200563 BINDING SITE, designated SEQ ID:43319, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65138] Another function of VGAM1929 is therefore inhibition of LOC200563 (Accession XM\_117251). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200563. LOC200609 (Accession XM\_117256) is another VGAM1929 host target gene. LOC200609 BINDING SITE1 and LOC200609 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC200609, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE1 and LOC200609 BINDING SITE2, designated SEQ ID:43329 and SEQ ID:43336 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65139] Another function of VGAM1929 is therefore inhibition of LOC200609 (Accession XM\_117256). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. LOC201182 (Accession XM\_117055) is another VGAM1929 host target gene. LOC201182 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC201182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201182 BINDING SITE, designated SEQ ID:43212, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65140] Another function of VGAM1929 is therefore inhibition of LOC201182 (Accession XM\_117055). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201182. LOC201868 (Accession XM\_114393) is another VGAM1929 host target gene. LOC201868 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201868, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201868 BINDING SITE, designated SEQ ID:42922, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65141] Another function of VGAM1929 is therefore inhibition of LOC201868 (Accession XM\_114393). Accordingly, utilities

of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201868. LOC201965 (Accession XM\_114412) is another VGAM1929 host target gene. LOC201965 BINDING SITE1 and LOC201965 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC201965, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201965 BINDING SITE1 and LOC201965 BINDING SITE2, designated SEQ ID:42932 and SEQ ID:42933 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65142] Another function of VGAM1929 is therefore inhibition of LOC201965 (Accession XM\_114412). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201965. LOC202802 (Accession XM\_114560) is another VGAM1929 host target gene. LOC202802 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202802, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202802 BINDING SITE, designated SEQ ID:42990, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65143] Another function of VGAM1929 is therefore inhibition of LOC202802 (Accession XM\_114560). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202802. LOC202934 (Accession XM\_117486) is another VGAM1929 host target gene. LOC202934 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202934 BINDING SITE, designated SEQ ID:43457, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65144] Another function of VGAM1929 is therefore inhibition of LOC202934 (Accession XM\_117486). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC202934. LOC203248 (Accession XM\_114659) is another VGAM1929 host target gene. LOC203248 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203248 BINDING SITE, designated SEQ ID:43021, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65145] Another function of VGAM1929 is therefore inhibition of LOC203248 (Accession XM\_114659). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203248. LOC203536 (Accession XM\_114716) is another VGAM1929 host target gene. LOC203536 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203536, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203536 BINDING SITE, designated SEQ ID:43057, to the nucleotide sequence of VGAM1929 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4640.

[65146] Another function of VGAM1929 is therefore inhibition of LOC203536 (Accession XM\_114716). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203536. LOC205327 (Accession XM\_115788) is another VGAM1929 host target gene. LOC205327 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC205327, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205327 BINDING SITE, designated SEQ ID:43107, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65147] Another function of VGAM1929 is therefore inhibition of LOC205327 (Accession XM\_115788). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205327. LOC219654 (Accession XM\_166095) is another VGAM1929 host target gene. LOC219654 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219654, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219654 BINDING SITE, designated SEQ ID:43880, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65148] Another function of VGAM1929 is therefore inhibition of LOC219654 (Accession XM\_166095). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219654. LOC219942 (Accession XM\_167790) is another VGAM1929 host target gene. LOC219942 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219942, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219942 BINDING SITE, designated SEQ ID:44828, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65149] Another function of VGAM1929 is therefore inhibition of LOC219942 (Accession XM\_167790). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC219942. LOC220469 (Accession XM\_084334) is another VGAM1929 host target gene. LOC220469 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220469, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220469 BINDING SITE, designated SEQ ID:37557, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65150] Another function of VGAM1929 is therefore inhibition of LOC220469 (Accession XM\_084334). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220469. LOC220635 (Accession XM\_165433) is another VGAM1929 host target gene. LOC220635 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220635 BINDING SITE, designated SEQ ID:43639, to

the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65151] Another function of VGAM1929 is therefore inhibition of LOC220635 (Accession XM\_165433). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220635. LOC220729 (Accession XM\_049575) is another VGAM1929 host target gene. LOC220729 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220729, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220729 BINDING SITE, designated SEQ ID:35447, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65152] Another function of VGAM1929 is therefore inhibition of LOC220729 (Accession XM\_049575). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220729. LOC220963 (Accession XM\_166145) is another VGAM1929 host target gene. LOC220963 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC220963, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220963 BINDING SITE, designated SEQ ID:43956, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65153] Another function of VGAM1929 is therefore inhibition of LOC220963 (Accession XM\_166145). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220963. LOC220988 (Accession XM\_165561) is another VGAM1929 host target gene. LOC220988 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220988 BINDING SITE, designated SEQ ID:43686, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65154] Another function of VGAM1929 is therefore inhibition of LOC220988 (Accession XM\_165561). Accordingly, utilities

of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220988. LOC221178 (Accession XM\_167936) is another VGAM1929 host target gene. LOC221178 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221178 BINDING SITE, designated SEQ ID:44931, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65155] Another function of VGAM1929 is therefore inhibition of LOC221178 (Accession XM\_167936). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221178. LOC221312 (Accession XM\_166314) is another VGAM1929 host target gene. LOC221312 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC221312 BINDING SITE, designated SEQ ID:44139, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65156] Another function of VGAM1929 is therefore inhibition of LOC221312 (Accession XM\_166314). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221312. LOC221814 (Accession XM\_168226) is another VGAM1929 host target gene. LOC221814 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221814, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221814 BINDING SITE, designated SEQ ID:45091, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65157] Another function of VGAM1929 is therefore inhibition of LOC221814 (Accession XM\_168226). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221814. LOC221815 (Accession XM\_168225) is another VGAM1929 host target gene. LOC221815 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221815, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221815 BINDING SITE, designated SEQ ID:45087, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65158] Another function of VGAM1929 is therefore inhibition of LOC221815 (Accession XM\_168225). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221815. LOC222070 (Accession XM\_168433) is another VGAM1929 host target gene. LOC222070 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222070 BINDING SITE, designated SEQ ID:45182, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65159] Another function of VGAM1929 is therefore inhibition of

LOC222070 (Accession XM\_168433). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222070. LOC222159 (Accession XM\_168421) is another VGAM1929 host target gene. LOC222159 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222159 BINDING SITE, designated SEQ ID:45148, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65160] Another function of VGAM1929 is therefore inhibition of LOC222159 (Accession XM\_168421). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222159. LOC222161 (Accession XM\_166596) is another VGAM1929 host target gene. LOC222161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC222161 BINDING SITE, designated SEQ ID:44582, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65161] Another function of VGAM1929 is therefore inhibition of LOC222161 (Accession XM\_166596). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222161. LOC222178 (Accession XM\_168453) is another VGAM1929 host target gene. LOC222178 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222178 BINDING SITE, designated SEQ ID:45189, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65162] Another function of VGAM1929 is therefore inhibition of LOC222178 (Accession XM\_168453). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222178. LOC222228 (Accession XM\_168627) is an-

other VGAM1929 host target gene. LOC222228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222228 BINDING SITE, designated SEQ ID:45276, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65163] Another function of VGAM1929 is therefore inhibition of LOC222228 (Accession XM\_168627). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222228. LOC222233 (Accession XM\_168560) is another VGAM1929 host target gene. LOC222233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222233 BINDING SITE, designated SEQ ID:45245, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65164] Another function of VGAM1929 is therefore inhibition of LOC222233 (Accession XM\_168560). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222233. LOC222237 (Accession XM\_168592) is another VGAM1929 host target gene. LOC222237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222237 BINDING SITE, designated SEQ ID:45271, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65165] Another function of VGAM1929 is therefore inhibition of LOC222237 (Accession XM\_168592). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222237. LOC222256 (Accession XM\_168571) is another VGAM1929 host target gene. LOC222256 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222256, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222256 BINDING SITE, designated SEQ ID:45249, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65166] Another function of VGAM1929 is therefore inhibition of LOC222256 (Accession XM\_168571). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222256. LOC253776 (Accession XM\_173240) is another VGAM1929 host target gene. LOC253776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253776 BINDING SITE, designated SEQ ID:46527, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65167] Another function of VGAM1929 is therefore inhibition of LOC253776 (Accession XM\_173240). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC253776. LOC253786 (Accession XM\_173109) is another VGAM1929 host target gene. LOC253786 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253786 BINDING SITE, designated SEQ ID:46364, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65168] Another function of VGAM1929 is therefore inhibition of LOC253786 (Accession XM\_173109). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253786. LOC253890 (Accession XM\_171016) is another VGAM1929 host target gene. LOC253890 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253890, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253890 BINDING SITE, designated SEQ ID:45785, to the nucleotide sequence of VGAM1929 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4640.

[65169] Another function of VGAM1929 is therefore inhibition of LOC253890 (Accession XM\_171016). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253890. LOC254532 (Accession XM\_172961) is another VGAM1929 host target gene. LOC254532 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254532 BINDING SITE, designated SEQ ID:46215, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65170] Another function of VGAM1929 is therefore inhibition of LOC254532 (Accession XM\_172961). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254532. LOC255045 (Accession XM\_171243) is another VGAM1929 host target gene. LOC255045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255045, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255045 BINDING SITE, designated SEQ ID:46036, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65171] Another function of VGAM1929 is therefore inhibition of LOC255045 (Accession XM\_171243). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255045. LOC255465 (Accession XM\_173206) is another VGAM1929 host target gene. LOC255465 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255465 BINDING SITE, designated SEQ ID:46450, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65172] Another function of VGAM1929 is therefore inhibition of LOC255465 (Accession XM\_173206). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC255465. LOC255515 (Accession XM\_171185) is another VGAM1929 host target gene. LOC255515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255515 BINDING SITE, designated SEQ ID:45962, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65173] Another function of VGAM1929 is therefore inhibition of LOC255515 (Accession XM\_171185). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255515. LOC255520 (Accession XM\_171073) is another VGAM1929 host target gene. LOC255520 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255520 BINDING SITE, designated SEQ ID:45882, to



the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65174] Another function of VGAM1929 is therefore inhibition of LOC255520 (Accession XM\_171073). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255520. LOC256867 (Accession XM\_170694) is another VGAM1929 host target gene. LOC256867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256867 BINDING SITE, designated SEQ ID:45478, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65175] Another function of VGAM1929 is therefore inhibition of LOC256867 (Accession XM\_170694). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256867. LOC257017 (Accession XM\_173227) is another VGAM1929 host target gene. LOC257017 BINDING SITE1 and LOC257017 BINDING SITE2 are HOST TARGET

binding sites found in untranslated regions of mRNA encoded by LOC257017, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257017 BINDING SITE1 and LOC257017 BINDING SITE2, designated SEQ ID:46493 and SEQ ID:46499 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65176] Another function of VGAM1929 is therefore inhibition of LOC257017 (Accession XM\_173227). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257017. LOC51631 (Accession XM\_042779) is another VGAM1929 host target gene. LOC51631 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51631, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51631 BINDING SITE, designated SEQ ID:33769, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65177] Another function of VGAM1929 is therefore inhibition of LOC51631 (Accession XM\_042779). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51631. LOC57149 (Accession NM\_020424) is another VGAM1929 host target gene. LOC57149 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC57149, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57149 BINDING SITE, designated SEQ ID:21682, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65178] Another function of VGAM1929 is therefore inhibition of LOC57149 (Accession NM\_020424). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57149. LOC84549 (Accession NM\_032509) is another VGAM1929 host target gene. LOC84549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC84549, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC84549 BINDING SITE, designated SEQ ID:26263, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65179] Another function of VGAM1929 is therefore inhibition of LOC84549 (Accession NM\_032509). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC84549. LOC90309 (Accession XM\_030830) is another VGAM1929 host target gene. LOC90309 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90309, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90309 BINDING SITE, designated SEQ ID:31152, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65180] Another function of VGAM1929 is therefore inhibition of LOC90309 (Accession XM\_030830). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90309. LOC90624 (Accession XM\_033003) is another VGAM1929 host target gene. LOC90624 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90624 BINDING SITE, designated SEQ ID:31817, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65181] Another function of VGAM1929 is therefore inhibition of LOC90624 (Accession XM\_033003). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90624. LOC91012 (Accession XM\_035503) is another VGAM1929 host target gene. LOC91012 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91012, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91012 BINDING SITE, designated SEQ ID:32282, to the nucleotide sequence of VGAM1929 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4640.

[65182] Another function of VGAM1929 is therefore inhibition of LOC91012 (Accession XM\_035503). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91012. LOC91250 (Accession XM\_037135) is another VGAM1929 host target gene. LOC91250 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91250, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91250 BINDING SITE, designated SEQ ID:32546, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65183] Another function of VGAM1929 is therefore inhibition of LOC91250 (Accession XM\_037135). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91250. LOC91300 (Accession NM\_138774) is another VGAM1929 host target gene. LOC91300 BINDING SITE1 and LOC91300 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

LOC91300, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91300 BINDING SITE1 and LOC91300 BINDING SITE2, designated SEQ ID:29007 and SEQ ID:45388 respectively, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65184] Another function of VGAM1929 is therefore inhibition of LOC91300 (Accession NM\_138774). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91300. LOC92231 (Accession XM\_043734) is another VGAM1929 host target gene. LOC92231 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92231 BINDING SITE, designated SEQ ID:34011, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65185] Another function of VGAM1929 is therefore inhibition of

LOC92231 (Accession XM\_043734). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92231. LOC92597 (Accession XM\_046066) is another VGAM1929 host target gene. LOC92597 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92597 BINDING SITE, designated SEQ ID:34674, to the nucleotide sequence of VGAM1929 RNA, herein designated VGAM RNA, also designated SEQ ID:4640.

[65186] Another function of VGAM1929 is therefore inhibition of LOC92597 (Accession XM\_046066). Accordingly, utilities of VGAM1929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92597. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1930 (VGAM1930) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes



is known in the art.

[65187] VGAM1930 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1930 was detected is described hereinabove with reference to Figs. 1–8.

[65188] VGAM1930 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM1930 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65189] VGAM1930 gene encodes a VGAM1930 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1930 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1930 precursor RNA is designated SEQ ID:1916, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1916 is located at position 150946 relative to the genome of Human Herpesvirus 4.

[65190] VGAM1930 precursor RNA folds onto itself, forming VGAM1930 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65191] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1930 folded precursor RNA into VGAM1930 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1930 RNA is designated SEQ ID:4641, and is provided hereinbelow with reference to the sequence listing part.

[65192] VGAM1930 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1930 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1930 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[65193] VGAM1930 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1930 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1930 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1930 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1930 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[65194] The complementary binding of VGAM1930 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1930 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1930 host target RNA into VGAM1930 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65195] It is appreciated that VGAM1930 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1930 host target genes. The mRNA of each one of this plurality of VGAM1930 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1930 RNA, herein designated VGAM RNA, and which when bound by VGAM1930 RNA causes inhibition of translation of respective one or more VGAM1930 host target proteins.

[65196] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1930 gene, herein designated VGAM GENE, on one

or more VGAM1930 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65197] It is yet further appreciated that a function of VGAM1930 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1930 correlate with, and may be deduced from, the identity of the host target genes which VGAM1930 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65198] Nucleotide sequences of the VGAM1930 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1930 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1930 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1930 are further described hereinbelow with reference to Table 1.

[65199] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1930 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1930 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65200] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1930 gene, herein designated VGAM is inhibition of expression of VGAM1930 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1930 correlate with, and may be deduced from, the identity of the target genes which VGAM1930 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65201] Chromosome 1 Open Reading Frame 34 (C1orf34, Acces-

sion XM\_027172) is a VGAM1930 host target gene. C1orf34 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1orf34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf34 BINDING SITE, designated SEQ ID:30435, to the nucleotide sequence of VGAM1930 RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65202] A function of VGAM1930 is therefore inhibition of Chromosome 1 Open Reading Frame 34 (C1orf34, Accession XM\_027172). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf34. FLJ14106 (Accession NM\_025067) is another VGAM1930 host target gene. FLJ14106 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14106 BINDING SITE, designated SEQ ID:24666, to the nucleotide sequence of VGAM1930

RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65203] Another function of VGAM1930 is therefore inhibition of FLJ14106 (Accession NM\_025067). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14106. GENX-3414 (Accession NM\_003943) is another VGAM1930 host target gene. GENX-3414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GENX-3414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GENX-3414 BINDING SITE, designated SEQ ID:10061, to the nucleotide sequence of VGAM1930 RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65204] Another function of VGAM1930 is therefore inhibition of GENX-3414 (Accession NM\_003943). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GENX-3414. Smith-Magenis Syndrome Chromosome Region, Candidate 5 (SMCR5, Accession NM\_144774) is another VGAM1930 host target gene. SMCR5 BINDING SITE is



HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMCR5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMCR5 BINDING SITE, designated SEQ ID:29566, to the nucleotide sequence of VGAM1930 RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65205] Another function of VGAM1930 is therefore inhibition of Smith-Magenis Syndrome Chromosome Region, Candidate 5 (SMCR5, Accession NM\_144774). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMCR5. Syntaphilin (SNPH, Accession NM\_014723) is another VGAM1930 host target gene. SNPH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNPH BINDING SITE, designated SEQ ID:16288, to the nucleotide sequence of VGAM1930 RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65206] Another function of VGAM1930 is therefore inhibition of Syntaphilin (SNPH, Accession NM\_014723). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNPH. LOC145845 (Accession XM\_096884) is another VGAM1930 host target gene. LOC145845 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145845, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145845 BINDING SITE, designated SEQ ID:40618, to the nucleotide sequence of VGAM1930 RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65207] Another function of VGAM1930 is therefore inhibition of LOC145845 (Accession XM\_096884). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145845. LOC146229 (Accession XM\_085387) is another VGAM1930 host target gene. LOC146229 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC146229, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146229 BINDING SITE, designated SEQ ID:38117, to the nucleotide sequence of VGAM1930 RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65208] Another function of VGAM1930 is therefore inhibition of LOC146229 (Accession XM\_085387). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146229. LOC148534 (Accession XM\_086222) is another VGAM1930 host target gene. LOC148534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148534 BINDING SITE, designated SEQ ID:38550, to the nucleotide sequence of VGAM1930 RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65209] Another function of VGAM1930 is therefore inhibition of LOC148534 (Accession XM\_086222). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC148534. LOC151201 (Accession XM\_098021) is another VGAM1930 host target gene. LOC151201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151201 BINDING SITE, designated SEQ ID:41326, to the nucleotide sequence of VGAM1930 RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65210] Another function of VGAM1930 is therefore inhibition of LOC151201 (Accession XM\_098021). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151201. LOC152991 (Accession XM\_098295) is another VGAM1930 host target gene. LOC152991 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152991, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152991 BINDING SITE, designated SEQ ID:41566, to the nucleotide sequence of VGAM1930 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4641.

[65211] Another function of VGAM1930 is therefore inhibition of LOC152991 (Accession XM\_098295). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152991. LOC57406 (Accession NM\_020676) is another VGAM1930 host target gene. LOC57406 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC57406, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57406 BINDING SITE, designated SEQ ID:21839, to the nucleotide sequence of VGAM1930 RNA, herein designated VGAM RNA, also designated SEQ ID:4641.

[65212] Another function of VGAM1930 is therefore inhibition of LOC57406 (Accession NM\_020676). Accordingly, utilities of VGAM1930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57406. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1931 (VGAM1931) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65213] VGAM1931 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1931 was detected is described hereinabove with reference to Figs. 1–8.

[65214] VGAM1931 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM1931 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65215] VGAM1931 gene encodes a VGAM1931 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1931 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1931 precursor RNA is designated SEQ ID:1917, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1917 is located at position 151629 relative to the genome of Human Herpesvirus 4.

[65216] VGAM1931 precursor RNA folds onto itself, forming

VGAM1931 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65217] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1931 folded precursor RNA into VGAM1931 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 74%) nucleotide sequence of VGAM1931 RNA is designated SEQ ID:4642, and is provided hereinbelow with reference to the sequence listing part.

[65218] VGAM1931 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1931 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1931 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65219] VGAM1931 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1931 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1931 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1931 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1931 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example



only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65220] The complementary binding of VGAM1931 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1931 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1931 host target RNA into VGAM1931 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65221] It is appreciated that VGAM1931 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1931 host target genes. The mRNA of each one of this plurality of VGAM1931 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1931 RNA, herein designated VGAM RNA, and which when bound by VGAM1931 RNA causes inhibition of translation of respective one or more VGAM1931 host target proteins.

[65222] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1931 gene, herein designated VGAM GENE, on one or more VGAM1931 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65223] It is yet further appreciated that a function of VGAM1931 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1931 correlate with, and may be deduced from, the identity of the host target genes which VGAM1931 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[65224] Nucleotide sequences of the VGAM1931 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1931 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1931 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1931 are further described hereinbelow with reference to Table 1.

[65225] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1931 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1931 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65226] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1931 gene, herein designated VGAM is inhibition of expression of VGAM1931 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1931 correlate with, and may be deduced from, the identity of the target genes which VGAM1931 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[65227] Collagen, Type VI, Alpha 1 (COL6A1, Accession NM\_001848) is a VGAM1931 host target gene. COL6A1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by COL6A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL6A1 BINDING SITE, designated SEQ ID:7584, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65228] A function of VGAM1931 is therefore inhibition of Collagen, Type VI, Alpha 1 (COL6A1, Accession NM\_001848). Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL6A1. HIP12 (Accession XM\_038791) is another VGAM1931 host target gene. HIP12 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HIP12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of HIP12 BINDING SITE, designated SEQ ID:32922, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65229] Another function of VGAM1931 is therefore inhibition of HIP12 (Accession XM\_038791), a gene which is a component of clathrin-coated pits and vesicles, that may link the endocytic machinery to the actin cytoskeleton. Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIP12. The function of HIP12 has been established by previous studies. Huntingtin-interacting protein-1 (HIP1; 601767) is a membrane-associated protein that interacts with huntingtin (OMIM Ref. No. 143100), the protein altered in Huntington disease. While attempting to isolate the mouse homolog of HIP1, Chopra et al. (2000) identified a homologous cDNA, which they designated Hip12. By screening a human frontal cortex cDNA library with an EST that showed homology to mouse Hip12, Chopra et al. (2000) cloned a full-length HIP12 cDNA encoding a deduced 1,068-amino acid protein that shares 47% sequence identity with HIP1. The highest degree of similarity occurs in the C-terminal region, which shows considerable homology to the cytoskeletal protein talin

(OMIM Ref. No. 186745). Northern blot analysis detected expression of a 5-kb HIP12 transcript in brain, heart, kidney, pancreas, and liver, but not in lung or placenta. In ES cell-derived neurons, both HIP1 and HIP12 are highly expressed and distributed throughout the cytoplasm and cell processes with enrichment within the cis-Golgi. In contrast to HIP1, which is toxic in cell culture, HIP12 does not confer toxicity in the same assay systems. HIP12 does not interact with huntingtin but can interact with HIP1, suggesting a potential interaction in vivo that may influence the function of each respective protein. By searching EST databases for homologs of yeast Sla2p, Engqvist-Goldstein et al. (1999) identified mouse and human cDNAs encoding HIP1R. The deduced human protein, which is 91% identical to the mouse sequence, is identical to the KIAA0655 protein reported by Ishikawa et al. (1998). It is also identical to the shorter sequence reported by Seki et al. (1998) except that it contains approximately 180 additional amino acids in its N terminus, including a conserved domain implicated in the endocytic function of Sla2p. HIP1R has 3 predicted coiled coils and a C-terminal talin-like domain, which Engqvist-Goldstein et al. (1999) confirmed binds F-actin in vitro. Northern blot analysis re-

vealed that mouse Hip1r is expressed ubiquitously, with reduced expression in skeletal muscle and heart, consistent with RT-PCR analysis of human HIP1R expression (Seki et al., 1998; Ishikawa et al., 1998). Fluorescence microscopy demonstrated that mouse Hip1r is expressed as punctate structures, enriched at the cell cortex and excluded from the nucleus, which colocalize with clathrin (see OMIM Ref. No. 118955) and other markers of receptor-mediated endocytosis.

[65230] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[65231] Chopra, V. S.; Metzler, M.; Rasper, D. M.; Engqvist-Goldstein, A. E. Y.; Singaraja, R.; Gan, L.; Fichter, K. M.; McCutcheon, K.; Drubin, D.; Nicholson, D. W.; Hayden, M. R. : HIP12 is a non-proapoptotic member of a gene family including HIP1, an interacting protein with huntingtin. Mammalian Genome 11: 1006-1015, 2000. ; and

[65232] Engqvist–Goldstein, A. E. Y.; Kessels, M. M.; Chopra, V. S.; Hayden, M. R.; Drubin, D. G. : An actin–binding protein of the Sla2/Huntingtin interacting protein 1 family is a novel compo.

[65233] Further studies establishing the function and utilities of HIP12 are found in John Hopkins OMIM database record ID 605613, and in cited publications numbered 717 and 9440–6775 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Splicing Factor, Arginine/serine–rich 1 (splicing factor 2, alternate splicing factor) (SFRS1, Accession NM\_006924) is another VGAM1931 host target gene. SFRS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SFRS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS1 BINDING SITE, designated SEQ ID:13801, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65234] Another function of VGAM1931 is therefore inhibition of Splicing Factor, Arginine/serine–rich 1 (splicing factor 2, alternate splicing factor) (SFRS1, Accession NM\_006924), a



gene which plays an essential role in pre-mRNA splicing. Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS1. The function of SFRS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM323.FLJ20436 (Accession NM\_017822) is another VGAM1931 host target gene. FLJ20436 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20436, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20436 BINDING SITE, designated SEQ ID:19472, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65235] Another function of VGAM1931 is therefore inhibition of FLJ20436 (Accession NM\_017822). Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20436. KIAA1622 (Accession NM\_058237) is another VGAM1931 host target gene. KIAA1622 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1622 BINDING SITE, designated SEQ ID:27766, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65236] Another function of VGAM1931 is therefore inhibition of KIAA1622 (Accession NM\_058237). Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1622. Zinc Finger Protein 212 (ZNF212, Accession NM\_012256) is another VGAM1931 host target gene. ZNF212 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF212, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF212 BINDING SITE, designated SEQ ID:14557, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65237] Another function of VGAM1931 is therefore inhibition of Zinc Finger Protein 212 (ZNF212, Accession NM\_012256). Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF212. LOC145761 (Accession XM\_096855) is another VGAM1931 host target gene. LOC145761 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145761 BINDING SITE, designated SEQ ID:40584, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65238] Another function of VGAM1931 is therefore inhibition of LOC145761 (Accession XM\_096855). Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145761. LOC146603 (Accession XM\_085514) is another VGAM1931 host target gene. LOC146603 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146603, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146603 BINDING SITE, designated SEQ ID:38215, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65239] Another function of VGAM1931 is therefore inhibition of LOC146603 (Accession XM\_085514). Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146603. LOC202986 (Accession XM\_117489) is another VGAM1931 host target gene. LOC202986 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202986, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202986 BINDING SITE, designated SEQ ID:43470, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65240] Another function of VGAM1931 is therefore inhibition of LOC202986 (Accession XM\_117489). Accordingly, utilities of VGAM1931 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC202986. LOC51312 (Accession NM\_018579) is another VGAM1931 host target gene. LOC51312 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51312 BINDING SITE, designated SEQ ID:20659, to the nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65241] Another function of VGAM1931 is therefore inhibition of LOC51312 (Accession NM\_018579). Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51312. LOC57105 (Accession NM\_020377) is another VGAM1931 host target gene. LOC57105 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC57105, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57105 BINDING SITE, designated SEQ ID:21639, to the

nucleotide sequence of VGAM1931 RNA, herein designated VGAM RNA, also designated SEQ ID:4642.

[65242] Another function of VGAM1931 is therefore inhibition of LOC57105 (Accession NM\_020377). Accordingly, utilities of VGAM1931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57105. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1932 (VGAM1932) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65243] VGAM1932 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1932 was detected is described hereinabove with reference to Figs. 1–8.

[65244] VGAM1932 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM1932 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65245] VGAM1932 gene encodes a VGAM1932 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1932 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1932 precursor RNA is designated SEQ ID:1918, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1918 is located at position 159902 relative to the genome of Human Herpesvirus 4.

[65246] VGAM1932 precursor RNA folds onto itself, forming VGAM1932 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65247] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1932 folded precursor RNA into VGAM1932 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1932 RNA is designated SEQ ID:4643, and is provided hereinbelow with reference to the sequence listing part.

[65248] VGAM1932 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1932 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1932 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65249] VGAM1932 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1932 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1932 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding



sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1932 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1932 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65250] The complementary binding of VGAM1932 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1932 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1932 host target RNA into VGAM1932 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65251] It is appreciated that VGAM1932 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1932 host target genes. The mRNA of each one of this plurality of VGAM1932 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1932 RNA, herein designated VGAM RNA, and which when bound by VGAM1932 RNA causes inhibition of translation of respective one or more VGAM1932 host target proteins.

[65252] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1932 gene, herein designated VGAM GENE, on one or more VGAM1932 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[65253] It is yet further appreciated that a function of VGAM1932 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1932 correlate with, and may be deduced from, the identity of the host target genes which VGAM1932 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65254] Nucleotide sequences of the VGAM1932 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1932 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1932 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1932 are further described hereinbelow with reference to Table 1.

[65255] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1932 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1932 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65256] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1932 gene, herein designated VGAM is inhibition of expression of VGAM1932 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1932 correlate with, and may be deduced from, the identity of the target genes which VGAM1932 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65257] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 4 (B4GALT4, Accession NM\_003778) is a VGAM1932 host target gene. B4GALT4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by B4GALT4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT4 BINDING SITE, designated SEQ ID:9858, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65258] A function of VGAM1932 is therefore inhibition of UDP-

Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 4 (B4GALT4, Accession NM\_003778). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT4. Glutamine-fructose-6-phosphate Transaminase 2 (GFPT2, Accession NM\_005110) is another VGAM1932 host target gene. GFPT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFPT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFPT2 BINDING SITE, designated SEQ ID:11594, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65259] Another function of VGAM1932 is therefore inhibition of Glutamine-fructose-6-phosphate Transaminase 2 (GFPT2, Accession NM\_005110). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFPT2. Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM\_005628) is another VGAM1932 host target gene. SLC1A5 BINDING SITE1 and

SLC1A5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC1A5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A5 BINDING SITE1 and SLC1A5 BINDING SITE2, designated SEQ ID:12142 and SEQ ID:38402 respectively, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65260] Another function of VGAM1932 is therefore inhibition of Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM\_005628). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A5. Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM\_029962) is another VGAM1932 host target gene. KCNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNT1 BINDING SITE, des-

ignated SEQ ID:30974, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65261] Another function of VGAM1932 is therefore inhibition of Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM\_029962). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNT1. KIAA0258 (Accession NM\_014785) is another VGAM1932 host target gene. KIAA0258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0258 BINDING SITE, designated SEQ ID:16648, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65262] Another function of VGAM1932 is therefore inhibition of KIAA0258 (Accession NM\_014785). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0258. KIAA0514 (Accession NM\_014696) is another

VGAM1932 host target gene. KIAA0514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0514 BINDING SITE, designated SEQ ID:16208, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65263] Another function of VGAM1932 is therefore inhibition of KIAA0514 (Accession NM\_014696). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0514. KIAA1987 (Accession XM\_113870) is another VGAM1932 host target gene. KIAA1987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1987 BINDING SITE, designated SEQ ID:42498, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.



[65264] Another function of VGAM1932 is therefore inhibition of KIAA1987 (Accession XM\_113870). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1987. MGC15854 (Accession NM\_145029) is another VGAM1932 host target gene. MGC15854 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15854 BINDING SITE, designated SEQ ID:29644, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65265] Another function of VGAM1932 is therefore inhibition of MGC15854 (Accession NM\_145029). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15854. MGC16279 (Accession XM\_031808) is another VGAM1932 host target gene. MGC16279 BINDING SITE1 and MGC16279 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MGC16279, corresponding to HOST TARGET

binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16279 BINDING SITE1 and MGC16279 BINDING SITE2, designated SEQ ID:31487 and SEQ ID:26733 respectively, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65266] Another function of VGAM1932 is therefore inhibition of MGC16279 (Accession XM\_031808). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16279. NY-REN-25 (Accession XM\_027116) is another VGAM1932 host target gene. NY-REN-25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NY-REN-25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-25 BINDING SITE, designated SEQ ID:30417, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65267] Another function of VGAM1932 is therefore inhibition of NY-REN-25 (Accession XM\_027116). Accordingly, utilities

of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-25. Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM\_047007) is another VGAM1932 host target gene. PLAGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAGL2 BINDING SITE, designated SEQ ID:34878, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65268] Another function of VGAM1932 is therefore inhibition of Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM\_047007). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAGL2. PRO0902 (Accession NM\_053057) is another VGAM1932 host target gene. PRO0902 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0902, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0902 BINDING SITE, designated SEQ ID:27609, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65269] Another function of VGAM1932 is therefore inhibition of PRO0902 (Accession NM\_053057). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0902. Sideroflexin 2 (SFXN2, Accession XM\_058359) is another VGAM1932 host target gene. SFXN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFXN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFXN2 BINDING SITE, designated SEQ ID:36604, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65270] Another function of VGAM1932 is therefore inhibition of Sideroflexin 2 (SFXN2, Accession XM\_058359). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with SFXN2. Ubc6p (Accession NM\_058167) is another VGAM1932 host target gene. Ubc6p BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Ubc6p, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Ubc6p BINDING SITE, designated SEQ ID:27715, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65271] Another function of VGAM1932 is therefore inhibition of Ubc6p (Accession NM\_058167). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Ubc6p. LOC157450 (Accession XM\_048209) is another VGAM1932 host target gene. LOC157450 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157450 BINDING SITE, designated SEQ ID:35148, to the nucleotide sequence of VGAM1932 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4643.

[65272] Another function of VGAM1932 is therefore inhibition of LOC157450 (Accession XM\_048209). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157450. LOC51336 (Accession NM\_016646) is another VGAM1932 host target gene. LOC51336 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51336 BINDING SITE, designated SEQ ID:18758, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65273] Another function of VGAM1932 is therefore inhibition of LOC51336 (Accession NM\_016646). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51336. LOC91409 (Accession XM\_038298) is another VGAM1932 host target gene. LOC91409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91409, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91409 BINDING SITE, designated SEQ ID:32805, to the nucleotide sequence of VGAM1932 RNA, herein designated VGAM RNA, also designated SEQ ID:4643.

[65274] Another function of VGAM1932 is therefore inhibition of LOC91409 (Accession XM\_038298). Accordingly, utilities of VGAM1932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91409. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1933 (VGAM1933) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65275] VGAM1933 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1933 was detected is described hereinabove with reference to Figs. 1-8.

[65276] VGAM1933 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4.

VGAM1933 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65277] VGAM1933 gene encodes a VGAM1933 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1933 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1933 precursor RNA is designated SEQ ID:1919, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1919 is located at position 156037 relative to the genome of Human Herpesvirus 4.

[65278] VGAM1933 precursor RNA folds onto itself, forming VGAM1933 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65279] An enzyme complex designated DICER COMPLEX, `dices`



the VGAM1933 folded precursor RNA into VGAM1933 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1933 RNA is designated SEQ ID:4644, and is provided hereinbelow with reference to the sequence listing part.

[65280] VGAM1933 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1933 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1933 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65281] VGAM1933 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1933 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1933 RNA is an accurate or a partial inversed–reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1933 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1933 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65282] The complementary binding of VGAM1933 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1933 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1933 host target RNA into VGAM1933 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65283] It is appreciated that VGAM1933 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1933 host target genes. The mRNA of each one of this plurality of VGAM1933 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1933 RNA, herein designated VGAM RNA, and which when bound by VGAM1933 RNA causes inhibition of translation of respective one or more VGAM1933 host target proteins.

[65284] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1933 gene, herein designated VGAM GENE, on one or more VGAM1933 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65285] It is yet further appreciated that a function of VGAM1933 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1933 correlate with, and may be deduced from, the identity of the host target genes which VGAM1933 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65286] Nucleotide sequences of the VGAM1933 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1933 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1933 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1933 are further described hereinbelow with reference to Table 1.

[65287] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1933 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1933 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65288] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1933 gene, herein designated VGAM is inhibition of expression of VGAM1933 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1933 correlate with, and may be deduced from, the identity of the target genes which VGAM1933 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65289] Cadherin 8, Type 2 (CDH8, Accession NM\_001796) is a VGAM1933 host target gene. CDH8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDH8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH8 BINDING SITE, designated SEQ ID:7550, to the nucleotide sequence of

VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65290] A function of VGAM1933 is therefore inhibition of Cadherin 8, Type 2 (CDH8, Accession NM\_001796), a gene which plays an important role in development and maintenance of tissues. Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH8. The function of CDH8 has been established by previous studies. Cadherins are integral membrane proteins that mediate calcium-dependent cell-cell adhesion. They are thought to play an important role in development and maintenance of tissues and may be involved in the invasion and metastasis of malignant tumors. Mature cadherin proteins are composed of a large N-terminal extracellular domain, a single membrane-spanning domain, and a small C-terminal cytoplasmic domain. The extracellular domain consists of 5 subdomains, each containing a cadherin motif, and appears to determine the specificity of the homophilic cell adhesion activity of the cadherin; the amino acid sequence of the cytoplasmic domain is highly conserved among cadherins. By PCR using degenerate oligonucleotides based on highly conserved sequences of

the cadherin cytoplasmic domain, followed by screening of a human fetal brain cDNA library, Suzuki et al. (1991) isolated a partial cDNA encoding CDH8. Northern blot analysis detected Cdh8 expression only in rat brain, with multiple transcripts present. Tanihara et al. (1994) isolated a human brain cDNA containing the entire coding sequence of CDH8. The predicted 793-amino acid CDH8 protein contains a signal sequence, prosequence, extracellular domain, transmembrane sequence, and cytoplasmic domain. The extracellular domain of CDH8 has 66%, 58%, and 40% amino acid identity with the extracellular domains of human CDH11 (OMIM Ref. No. 600023), CDH12 (OMIM Ref. No. 600562), and CDH5 (OMIM Ref. No. 601120), respectively

[65291] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[65292] Kremmidiotis, G.; Baker, E.; Crawford, J.; Eyre, H. J.; Nahmias, J.; Callen, D. F. : Localization of human cadherin genes to chromosome regions exhibiting cancer-related loss of heterozygosity. *Genomics* 49: 467-471, 1998. ; and

[65293] Suzuki, S.; Sano, K.; Tanihara, H. : Diversity of the cad-

herin family: evidence for eight new cadherins in nervous tissue. *Cell Regul.* 2: 261–270, 1991.

[65294] Further studies establishing the function and utilities of CDH8 are found in John Hopkins OMIM database record ID 603008, and in cited publications numbered 1164 and 8336 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate Receptor, Metabotropic 7 (GRM7, Accession NM\_000844) is another VGAM1933 host target gene. GRM7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRM7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM7 BINDING SITE, designated SEQ ID:6516, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65295] Another function of VGAM1933 is therefore inhibition of Glutamate Receptor, Metabotropic 7 (GRM7, Accession NM\_000844), a gene which is mediated by a g-protein that inhibits adenylate cyclase activity. Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated



with GRM7. The function of GRM7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM746. Molybdenum Cofactor Synthesis 1 (MOCS1, Accession XM\_166358) is another VGAM1933 host target gene. MOCS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MOCS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOCS1 BINDING SITE, designated SEQ ID:44186, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65296] Another function of VGAM1933 is therefore inhibition of Molybdenum Cofactor Synthesis 1 (MOCS1, Accession XM\_166358). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOCS1. Neuralized-like (Drosophila) (NEURL, Accession NM\_004210) is another VGAM1933 host target gene. NEURL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEURL, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEURL BINDING SITE, designated SEQ ID:10410, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65297] Another function of VGAM1933 is therefore inhibition of Neuralized-like (Drosophila) (NEURL, Accession NM\_004210). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEURL. Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754) is another VGAM1933 host target gene. RUNX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RUNX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RUNX1 BINDING SITE, designated SEQ ID:7495, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65298] Another function of VGAM1933 is therefore inhibition of

Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM\_001754). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RUNX1. Tripartite Motif-containing 8 (TRIM8, Accession NM\_030912) is another VGAM1933 host target gene. TRIM8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM8 BINDING SITE, designated SEQ ID:25179, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65299] Another function of VGAM1933 is therefore inhibition of Tripartite Motif-containing 8 (TRIM8, Accession NM\_030912). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM8. Aldehyde Dehydrogenase 5 Family, Member A1 (succinate-semialdehyde dehydrogenase) (ALDH5A1, Accession NM\_001080) is another VGAM1933 host target gene. ALDH5A1 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALDH5A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH5A1 BINDING SITE, designated SEQ ID:6740, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65300] Another function of VGAM1933 is therefore inhibition of Aldehyde Dehydrogenase 5 Family, Member A1 (succinate-semialdehyde dehydrogenase) (ALDH5A1, Accession NM\_001080). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH5A1. Chromosome 22 Open Reading Frame 20 (C22orf20, Accession NM\_025225) is another VGAM1933 host target gene. C22orf20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C22orf20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf20 BINDING SITE, designated SEQ ID:24902, to the nucleotide sequence of VGAM1933 RNA,

herein designated VGAM RNA, also designated SEQ ID:4644.

[65301] Another function of VGAM1933 is therefore inhibition of Chromosome 22 Open Reading Frame 20 (C22orf20, Accession NM\_025225). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf20.

FLJ22969 (Accession XM\_044006) is another VGAM1933 host target gene. FLJ22969 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22969, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22969 BINDING SITE, designated SEQ ID:34064, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65302] Another function of VGAM1933 is therefore inhibition of FLJ22969 (Accession XM\_044006). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22969. KIAA0441 (Accession NM\_014797) is another VGAM1933 host target gene. KIAA0441 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0441 BINDING SITE, designated SEQ ID:16707, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65303] Another function of VGAM1933 is therefore inhibition of KIAA0441 (Accession NM\_014797). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0441. KIAA1265 (Accession XM\_047707) is another VGAM1933 host target gene. KIAA1265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1265 BINDING SITE, designated SEQ ID:35031, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65304] Another function of VGAM1933 is therefore inhibition of

KIAA1265 (Accession XM\_047707). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1265. KIAA1789 (Accession XM\_040486) is another VGAM1933 host target gene. KIAA1789 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1789 BINDING SITE, designated SEQ ID:33309, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65305] Another function of VGAM1933 is therefore inhibition of KIAA1789 (Accession XM\_040486). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1789. NFASC (Accession XM\_046808) is another VGAM1933 host target gene. NFASC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFASC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of NFASC BINDING SITE, designated SEQ ID:34827, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65306] Another function of VGAM1933 is therefore inhibition of NFASC (Accession XM\_046808). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFASC. Paired Mesoderm Homeobox 2b (PMX2B, Accession NM\_003924) is another VGAM1933 host target gene. PMX2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMX2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMX2B BINDING SITE, designated SEQ ID:10013, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65307] Another function of VGAM1933 is therefore inhibition of Paired Mesoderm Homeobox 2b (PMX2B, Accession NM\_003924). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clini-



cal conditions associated with PMX2B. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM\_028840) is another VGAM1933 host target gene. PPP1R16B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R16B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R16B BINDING SITE, designated SEQ ID:30766, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65308] Another function of VGAM1933 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM\_028840). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R16B. LOC146138 (Accession XM\_096938) is another VGAM1933 host target gene. LOC146138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC146138 BINDING SITE, designated SEQ ID:40653, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65309] Another function of VGAM1933 is therefore inhibition of LOC146138 (Accession XM\_096938). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146138. LOC146332 (Accession XM\_085413) is another VGAM1933 host target gene. LOC146332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146332 BINDING SITE, designated SEQ ID:38127, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65310] Another function of VGAM1933 is therefore inhibition of LOC146332 (Accession XM\_085413). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146332. LOC150311 (Accession XM\_086858) is an-

other VGAM1933 host target gene. LOC150311 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150311, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150311 BINDING SITE, designated SEQ ID:38927, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65311] Another function of VGAM1933 is therefore inhibition of LOC150311 (Accession XM\_086858). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150311. LOC150383 (Accession XM\_086905) is another VGAM1933 host target gene. LOC150383 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150383, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150383 BINDING SITE, designated SEQ ID:38944, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65312] Another function of VGAM1933 is therefore inhibition of LOC150383 (Accession XM\_086905). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150383. LOC154449 (Accession XM\_087928) is another VGAM1933 host target gene. LOC154449 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154449 BINDING SITE, designated SEQ ID:39474, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65313] Another function of VGAM1933 is therefore inhibition of LOC154449 (Accession XM\_087928). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154449. LOC158654 (Accession XM\_088632) is another VGAM1933 host target gene. LOC158654 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158654, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158654 BINDING SITE, designated SEQ ID:39875, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65314] Another function of VGAM1933 is therefore inhibition of LOC158654 (Accession XM\_088632). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158654. LOC253443 (Accession XM\_171074) is another VGAM1933 host target gene. LOC253443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253443 BINDING SITE, designated SEQ ID:45883, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65315] Another function of VGAM1933 is therefore inhibition of LOC253443 (Accession XM\_171074). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC253443. LOC255388 (Accession XM\_173161) is another VGAM1933 host target gene. LOC255388 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255388, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255388 BINDING SITE, designated SEQ ID:46418, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65316] Another function of VGAM1933 is therefore inhibition of LOC255388 (Accession XM\_173161). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255388. LOC256310 (Accession XM\_172813) is another VGAM1933 host target gene. LOC256310 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256310 BINDING SITE, designated SEQ ID:46095, to the nucleotide sequence of VGAM1933 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4644.

[65317] Another function of VGAM1933 is therefore inhibition of LOC256310 (Accession XM\_172813). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256310. LOC51701 (Accession NM\_016231) is another VGAM1933 host target gene. LOC51701 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51701, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51701 BINDING SITE, designated SEQ ID:18345, to the nucleotide sequence of VGAM1933 RNA, herein designated VGAM RNA, also designated SEQ ID:4644.

[65318] Another function of VGAM1933 is therefore inhibition of LOC51701 (Accession NM\_016231). Accordingly, utilities of VGAM1933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51701. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1934 (VGAM1934) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65319] VGAM1934 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1934 was detected is described hereinabove with reference to Figs. 1–8.

[65320] VGAM1934 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM1934 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65321] VGAM1934 gene encodes a VGAM1934 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1934 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1934 precursor RNA is designated SEQ ID:1920, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1920 is located at position 157308 relative to the genome of Human Herpesvirus 4.

[65322] VGAM1934 precursor RNA folds onto itself, forming



VGAM1934 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65323] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1934 folded precursor RNA into VGAM1934 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM1934 RNA is designated SEQ ID:4645, and is provided hereinbelow with reference to the sequence listing part.

[65324] VGAM1934 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1934 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1934 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65325] VGAM1934 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1934 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1934 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1934 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1934 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65326] The complementary binding of VGAM1934 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1934 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1934 host target RNA into VGAM1934 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65327] It is appreciated that VGAM1934 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1934 host target genes. The mRNA of each one of this plurality of VGAM1934 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1934 RNA, herein designated VGAM RNA, and which when bound by VGAM1934 RNA causes inhibition of translation of respective one or more VGAM1934 host target proteins.

[65328] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1934 gene, herein designated VGAM GENE, on one or more VGAM1934 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65329] It is yet further appreciated that a function of VGAM1934 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1934 correlate with, and may be deduced from, the identity of the host target genes which VGAM1934 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[65330] Nucleotide sequences of the VGAM1934 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1934 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1934 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1934 are further described hereinbelow with reference to Table 1.

[65331] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1934 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1934 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65332] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1934 gene, herein designated VGAM is inhibition of expression of VGAM1934 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1934 correlate with, and may be deduced from, the identity of the target genes which VGAM1934 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[65333] Acyl-Coenzyme A Dehydrogenase, Short/branched Chain (ACADSB, Accession NM\_001609) is a VGAM1934 host target gene. ACADSB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACADSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACADSB BINDING SITE, designated SEQ ID:7315, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65334] A function of VGAM1934 is therefore inhibition of Acyl-Coenzyme A Dehydrogenase, Short/branched Chain (ACADSB, Accession NM\_001609). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACADSB. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3A (glycogen and sarcoplasmic reticulum binding subunit, skeletal muscle) (PPP1R3A, Accession NM\_002711) is another VGAM1934 host target gene. PPP1R3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

PPP1R3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R3A BINDING SITE, designated SEQ ID:8563, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65335] Another function of VGAM1934 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3A (glycogen and sarcoplasmic reticulum binding subunit, skeletal muscle) (PPP1R3A, Accession NM\_002711), a gene which regulates phosphatase activity towards glycogen synthase, active in skeletal muscle. Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R3A. The function of PPP1R3A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1872.DKFZP564C103 (Accession NM\_015654) is another VGAM1934 host target gene. DKFZP564C103 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564C103, corresponding to a HOST TARGET bind-

ing site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564C103 BINDING SITE, designated SEQ ID:17900, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65336] Another function of VGAM1934 is therefore inhibition of DKFZP564C103 (Accession NM\_015654). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564C103. FLJ22479 (Accession NM\_024900) is another VGAM1934 host target gene. FLJ22479 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22479 BINDING SITE, designated SEQ ID:24384, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65337] Another function of VGAM1934 is therefore inhibition of FLJ22479 (Accession NM\_024900). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment



of diseases and clinical conditions associated with FLJ22479. Ganglioside Induced Differentiation Associated Protein 2 (GDAP2, Accession NM\_017686) is another VGAM1934 host target gene. GDAP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GDAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GDAP2 BINDING SITE, designated SEQ ID:19239, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65338] Another function of VGAM1934 is therefore inhibition of Ganglioside Induced Differentiation Associated Protein 2 (GDAP2, Accession NM\_017686). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GDAP2. KIAA1317 (Accession XM\_098368) is another VGAM1934 host target gene. KIAA1317 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA1317 BINDING SITE, designated SEQ ID:41629, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65339] Another function of VGAM1934 is therefore inhibition of KIAA1317 (Accession XM\_098368). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1317. Melanoma Antigen, Family B, 1 (MAGEB1, Accession NM\_002363) is another VGAM1934 host target gene. MAGEB1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAGEB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAGEB1 BINDING SITE, designated SEQ ID:8174, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65340] Another function of VGAM1934 is therefore inhibition of Melanoma Antigen, Family B, 1 (MAGEB1, Accession NM\_002363). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with MAGEB1. MISS (Accession NM\_144578) is another VGAM1934 host target gene. MISS BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MISS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MISS BINDING SITE, designated SEQ ID:29382, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65341] Another function of VGAM1934 is therefore inhibition of MISS (Accession NM\_144578). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MISS. LOC126669 (Accession XM\_060121) is another VGAM1934 host target gene. LOC126669 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC126669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126669 BINDING SITE, designated SEQ ID:37156, to the nucleotide sequence of VGAM1934 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4645.

[65342] Another function of VGAM1934 is therefore inhibition of LOC126669 (Accession XM\_060121). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126669. LOC149670 (Accession XM\_086647) is another VGAM1934 host target gene. LOC149670 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149670, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149670 BINDING SITE, designated SEQ ID:38805, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65343] Another function of VGAM1934 is therefore inhibition of LOC149670 (Accession XM\_086647). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149670. LOC150174 (Accession XM\_086802) is another VGAM1934 host target gene. LOC150174 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150174, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150174 BINDING SITE, designated SEQ ID:38870, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65344] Another function of VGAM1934 is therefore inhibition of LOC150174 (Accession XM\_086802). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150174. LOC153894 (Accession XM\_087796) is another VGAM1934 host target gene. LOC153894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153894 BINDING SITE, designated SEQ ID:39426, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65345] Another function of VGAM1934 is therefore inhibition of LOC153894 (Accession XM\_087796). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC153894. LOC161357 (Accession XM\_090827) is another VGAM1934 host target gene. LOC161357 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC161357, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161357 BINDING SITE, designated SEQ ID:40018, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65346] Another function of VGAM1934 is therefore inhibition of LOC161357 (Accession XM\_090827). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161357. LOC255452 (Accession XM\_174088) is another VGAM1934 host target gene. LOC255452 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC255452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255452 BINDING SITE, designated SEQ ID:46571, to

the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65347] Another function of VGAM1934 is therefore inhibition of LOC255452 (Accession XM\_174088). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255452. LOC51652 (Accession NM\_016079) is another VGAM1934 host target gene. LOC51652 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51652, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51652 BINDING SITE, designated SEQ ID:18151, to the nucleotide sequence of VGAM1934 RNA, herein designated VGAM RNA, also designated SEQ ID:4645.

[65348] Another function of VGAM1934 is therefore inhibition of LOC51652 (Accession NM\_016079). Accordingly, utilities of VGAM1934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51652. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1935 (VGAM1935) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65349] VGAM1935 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1935 was detected is described hereinabove with reference to Figs. 1–8.

[65350] VGAM1935 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM1935 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65351] VGAM1935 gene encodes a VGAM1935 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1935 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1935 precursor RNA is designated SEQ ID:1921, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1921 is located at position 155556 relative to the genome of Human Herpesvirus 4.



[65352] VGAM1935 precursor RNA folds onto itself, forming VGAM1935 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65353] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1935 folded precursor RNA into VGAM1935 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1935 RNA is designated SEQ ID:4646, and is provided hereinbelow with reference to the sequence listing part.

[65354] VGAM1935 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1935 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1935 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65355] VGAM1935 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1935 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1935 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1935 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1935 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65356] The complementary binding of VGAM1935 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1935 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1935 host target RNA into VGAM1935 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65357] It is appreciated that VGAM1935 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1935 host target genes. The mRNA of each one of this plurality of VGAM1935 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1935 RNA, herein designated VGAM RNA, and which when bound by VGAM1935 RNA causes inhibition of translation of respective one or more VGAM1935 host target proteins.

[65358] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1935 gene, herein designated VGAM GENE, on one or more VGAM1935 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65359] It is yet further appreciated that a function of VGAM1935 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1935 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1935 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65360] Nucleotide sequences of the VGAM1935 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1935 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1935 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1935 are further described hereinbelow with reference to Table 1.

[65361] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1935 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1935 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65362] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1935 gene, herein designated VGAM is inhibition of expression of VGAM1935 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1935 correlate with, and may be deduced from, the identity of the target genes which VGAM1935

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65363] Carbonic Anhydrase XII (CA12, Accession NM\_001218) is a VGAM1935 host target gene. CA12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CA12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CA12 BINDING SITE, designated SEQ ID:6880, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65364] A function of VGAM1935 is therefore inhibition of Carbonic Anhydrase XII (CA12, Accession NM\_001218), a gene which functions in cellular transport and metabolic processes. Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CA12. The function of CA12 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM508. Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM\_033096) is another VGAM1935 host target gene. CLTCL1 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLTCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLTCL1 BINDING SITE, designated SEQ ID:31836, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65365] Another function of VGAM1935 is therefore inhibition of Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM\_033096), a gene which is involved in vesicle budding. Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLTCL1. The function of CLTCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42. Casein Kinase 1, Gamma 3 (CSNK1G3, Accession NM\_004384) is another VGAM1935 host target gene. CSNK1G3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CSNK1G3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of CSNK1G3 BINDING SITE, designated SEQ ID:10612, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65366] Another function of VGAM1935 is therefore inhibition of Casein Kinase 1, Gamma 3 (CSNK1G3, Accession NM\_004384). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSNK1G3. Endometrial Bleeding Associated Factor (left-right determination, factor A; transforming growth factor beta superfamily) (EBAF, Accession XM\_037302) is another VGAM1935 host target gene. EBAF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EBAF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EBAF BINDING SITE, designated SEQ ID:32610, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65367] Another function of VGAM1935 is therefore inhibition of Endometrial Bleeding Associated Factor (left-right determination, factor A; transforming growth factor beta su-



perfamily) (EBAF, Accession XM\_037302), a gene which LEFT–RIGHT AXIS MALFORMATIONS. Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EBAF. The function of EBAF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM93. Glucagon–like Peptide 1 Receptor (GLP1R, Accession NM\_002062) is another VGAM1935 host target gene. GLP1R BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GLP1R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLP1R BINDING SITE, designated SEQ ID:7824, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65368] Another function of VGAM1935 is therefore inhibition of Glucagon–like Peptide 1 Receptor (GLP1R, Accession NM\_002062), a gene which is mediated by g proteins which activate adenylyl cyclase. Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with GLP1R. The function of GLP1R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1652. Interleukin 10 Receptor, Alpha (IL10RA, Accession XM\_006447) is another VGAM1935 host target gene. IL10RA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL10RA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL10RA BINDING SITE, designated SEQ ID:30000, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65369] Another function of VGAM1935 is therefore inhibition of Interleukin 10 Receptor, Alpha (IL10RA, Accession XM\_006447), a gene which is a receptor for il-10. Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL10RA. The function of IL10RA and its association with various diseases and clinical conditions, has been established by previous studies, as described here-

in above with reference to VGAM134. Myeloproliferative Leukemia Virus Oncogene (MPL, Accession NM\_005373) is another VGAM1935 host target gene. MPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPL BINDING SITE, designated SEQ ID:11850, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65370] Another function of VGAM1935 is therefore inhibition of Myeloproliferative Leukemia Virus Oncogene (MPL, Accession NM\_005373). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPL. ARNTL2 (Accession NM\_020183) is another VGAM1935 host target gene. ARNTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARNTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNTL2 BINDING SITE, designated SEQ

ID:21418, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65371] Another function of VGAM1935 is therefore inhibition of ARNTL2 (Accession NM\_020183). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNTL2. BCL2-like 1 (BCL2L1, Accession NM\_138578) is another VGAM1935 host target gene. BCL2L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2L1 BINDING SITE, designated SEQ ID:28894, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65372] Another function of VGAM1935 is therefore inhibition of BCL2-like 1 (BCL2L1, Accession NM\_138578). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2L1. Casein Kinase 1, Gamma 1 (CSNK1G1, Accession NM\_022048) is another VGAM1935 host target

gene. CSNK1G1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CSNK1G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSNK1G1 BINDING SITE, designated SEQ ID:22570, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65373] Another function of VGAM1935 is therefore inhibition of Casein Kinase 1, Gamma 1 (CSNK1G1, Accession NM\_022048). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSNK1G1. DKFZP566G1424 (Accession XM\_097771) is another VGAM1935 host target gene. DKFZP566G1424 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP566G1424, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566G1424 BINDING SITE, designated SEQ ID:41117, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM

RNA, also designated SEQ ID:4646.

[65374] Another function of VGAM1935 is therefore inhibition of DKFZP566G1424 (Accession XM\_097771). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566G1424. DKFZp586I021 (Accession NM\_032271) is another VGAM1935 host target gene. DKFZp586I021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp586I021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586I021 BINDING SITE, designated SEQ ID:26025, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65375] Another function of VGAM1935 is therefore inhibition of DKFZp586I021 (Accession NM\_032271). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp586I021. FLJ12547 (Accession NM\_024992) is another VGAM1935 host target gene. FLJ12547 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by FLJ12547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12547 BINDING SITE, designated SEQ ID:24549, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65376] Another function of VGAM1935 is therefore inhibition of FLJ12547 (Accession NM\_024992). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12547. FLJ20281 (Accession XM\_165663) is another VGAM1935 host target gene. FLJ20281 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20281 BINDING SITE, designated SEQ ID:43729, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65377] Another function of VGAM1935 is therefore inhibition of FLJ20281 (Accession XM\_165663). Accordingly, utilities of

VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20281. FLJ22341 (Accession NM\_024599) is another VGAM1935 host target gene. FLJ22341 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ22341, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22341 BINDING SITE, designated SEQ ID:23848, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65378] Another function of VGAM1935 is therefore inhibition of FLJ22341 (Accession NM\_024599). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22341. HEMK (Accession NM\_016173) is another VGAM1935 host target gene. HEMK BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HEMK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEMK BINDING SITE,



designated SEQ ID:18271, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65379] Another function of VGAM1935 is therefore inhibition of HEMK (Accession NM\_016173). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEMK. Potassium Voltage-gated Channel, Shal-related Subfamily, Member 1 (KCND1, Accession NM\_004979) is another VGAM1935 host target gene. KCND1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCND1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCND1 BINDING SITE, designated SEQ ID:11427, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65380] Another function of VGAM1935 is therefore inhibition of Potassium Voltage-gated Channel, Shal-related Subfamily, Member 1 (KCND1, Accession NM\_004979). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with KCND1. KIAA0939 (Accession XM\_030524) is another VGAM1935 host target gene. KIAA0939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0939 BINDING SITE, designated SEQ ID:31063, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65381] Another function of VGAM1935 is therefore inhibition of KIAA0939 (Accession XM\_030524). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0939. KIAA1199 (Accession XM\_051860) is another VGAM1935 host target gene. KIAA1199 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1199, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1199 BINDING SITE, designated SEQ ID:35899, to the nucleotide sequence of VGAM1935 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4646.

[65382] Another function of VGAM1935 is therefore inhibition of KIAA1199 (Accession XM\_051860). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1199. KIAA1280 (Accession XM\_045766) is another VGAM1935 host target gene. KIAA1280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1280 BINDING SITE, designated SEQ ID:34550, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65383] Another function of VGAM1935 is therefore inhibition of KIAA1280 (Accession XM\_045766). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1280. Kelch-like 6 (Drosophila) (KLHL6, Accession NM\_130446) is another VGAM1935 host target gene. KLHL6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL6,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL6 BINDING SITE, designated SEQ ID:28214, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65384] Another function of VGAM1935 is therefore inhibition of Kelch-like 6 (*Drosophila*) (KLHL6, Accession NM\_130446). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL6. Karyopherin Alpha 6 (importin alpha 7) (KPNA6, Accession NM\_012316) is another VGAM1935 host target gene. KPNA6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KPNA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KPNA6 BINDING SITE, designated SEQ ID:14690, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65385] Another function of VGAM1935 is therefore inhibition of

Karyopherin Alpha 6 (importin alpha 7) (KPNA6, Accession NM\_012316). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KPNA6. MBLL39 (Accession NM\_005757) is another VGAM1935 host target gene.

MBLL39 BINDING SITE1 and MBLL39 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MBLL39, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBLL39 BINDING SITE1 and MBLL39 BINDING SITE2, designated SEQ ID:12319 and SEQ ID:29576 respectively, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65386] Another function of VGAM1935 is therefore inhibition of MBLL39 (Accession NM\_005757). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBLL39. P66 (Accession NM\_020699) is another VGAM1935 host target gene. P66 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P66, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P66 BINDING SITE, designated SEQ ID:21846, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65387] Another function of VGAM1935 is therefore inhibition of P66 (Accession NM\_020699). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P66. Sialyltransferase 4B (beta-galactoside alpha-2,3-sialyltransferase) (SIAT4B, Accession NM\_006927) is another VGAM1935 host target gene. SIAT4B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SIAT4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT4B BINDING SITE, designated SEQ ID:13813, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65388] Another function of VGAM1935 is therefore inhibition of Sialyltransferase 4B (beta-galactoside alpha-

2,3-sialyltransferase) (SIAT4B, Accession NM\_006927). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT4B. SSB-4 (Accession NM\_080862) is another VGAM1935 host target gene. SSB-4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSB-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSB-4 BINDING SITE, designated SEQ ID:28105, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65389] Another function of VGAM1935 is therefore inhibition of SSB-4 (Accession NM\_080862). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSB-4. UBE3B (Accession XM\_084941) is another VGAM1935 host target gene. UBE3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of UBE3B BINDING SITE, designated SEQ ID:37774, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65390] Another function of VGAM1935 is therefore inhibition of UBE3B (Accession XM\_084941). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE3B. LOC129198 (Accession XM\_072197) is another VGAM1935 host target gene. LOC129198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129198 BINDING SITE, designated SEQ ID:37466, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65391] Another function of VGAM1935 is therefore inhibition of LOC129198 (Accession XM\_072197). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129198. LOC158972 (Accession XM\_099009) is an-



other VGAM1935 host target gene. LOC158972 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158972, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158972 BINDING SITE, designated SEQ ID:42044, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65392] Another function of VGAM1935 is therefore inhibition of LOC158972 (Accession XM\_099009). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158972. LOC164395 (Accession XM\_092778) is another VGAM1935 host target gene. LOC164395 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164395, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164395 BINDING SITE, designated SEQ ID:40146, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65393] Another function of VGAM1935 is therefore inhibition of LOC164395 (Accession XM\_092778). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164395. LOC200261 (Accession XM\_114172) is another VGAM1935 host target gene. LOC200261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200261 BINDING SITE, designated SEQ ID:42750, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65394] Another function of VGAM1935 is therefore inhibition of LOC200261 (Accession XM\_114172). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200261. LOC221683 (Accession XM\_168089) is another VGAM1935 host target gene. LOC221683 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221683, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221683 BINDING SITE, designated SEQ ID:45006, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65395] Another function of VGAM1935 is therefore inhibition of LOC221683 (Accession XM\_168089). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221683. LOC254428 (Accession XM\_170932) is another VGAM1935 host target gene. LOC254428 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254428, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254428 BINDING SITE, designated SEQ ID:45720, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65396] Another function of VGAM1935 is therefore inhibition of LOC254428 (Accession XM\_170932). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC254428. LOC84549 (Accession NM\_032509) is another VGAM1935 host target gene. LOC84549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC84549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC84549 BINDING SITE, designated SEQ ID:26264, to the nucleotide sequence of VGAM1935 RNA, herein designated VGAM RNA, also designated SEQ ID:4646.

[65397] Another function of VGAM1935 is therefore inhibition of LOC84549 (Accession NM\_032509). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC84549. LOC91056 (Accession XM\_170662) is another VGAM1935 host target gene. LOC91056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91056 BINDING SITE, designated SEQ ID:45440, to the nucleotide sequence of VGAM1935 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4646.

[65398] Another function of VGAM1935 is therefore inhibition of LOC91056 (Accession XM\_170662). Accordingly, utilities of VGAM1935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91056. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1936 (VGAM1936) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65399] VGAM1936 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1936 was detected is described hereinabove with reference to Figs. 1–8.

[65400] VGAM1936 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM1936 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65401] VGAM1936 gene encodes a VGAM1936 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1936 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1936 precursor RNA is designated SEQ ID:1922, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1922 is located at position 152064 relative to the genome of Human Herpesvirus 4.

[65402] VGAM1936 precursor RNA folds onto itself, forming VGAM1936 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65403] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1936 folded precursor RNA into VGAM1936 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1936 RNA is designated SEQ ID:4647, and is provided hereinbelow with reference to the sequence listing part.

[65404] VGAM1936 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1936 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1936 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65405] VGAM1936 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1936 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1936 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1936 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1936 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[65406] The complementary binding of VGAM1936 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1936 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1936 host target RNA into VGAM1936 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65407] It is appreciated that VGAM1936 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1936 host target genes. The mRNA of



each one of this plurality of VGAM1936 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1936 RNA, herein designated VGAM RNA, and which when bound by VGAM1936 RNA causes inhibition of translation of respective one or more VGAM1936 host target proteins.

[65408] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1936 gene, herein designated VGAM GENE, on one or more VGAM1936 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[65409] It is yet further appreciated that a function of VGAM1936 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1936 correlate with, and may be deduced from, the identity of the host target genes which VGAM1936 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65410] Nucleotide sequences of the VGAM1936 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1936 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1936 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1936 are further described hereinbelow with reference to Table 1.

[65411] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1936 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1936 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65412] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1936 gene, herein designated VGAM is inhibition of expression of VGAM1936 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1936 correlate with, and may be deduced from, the identity of the target genes which VGAM1936 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65413] Adrenergic, Beta-3-, Receptor (ADRB3, Accession NM\_000025) is a VGAM1936 host target gene. ADRB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADRB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADRB3 BINDING SITE, designated SEQ ID:5463, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65414] A function of VGAM1936 is therefore inhibition of Adrenergic, Beta-3-, Receptor (ADRB3, Accession NM\_000025), a gene which stimulates adenylyl cyclase activity and reg-

ulates lipolysis. Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADRB3. The function of ADRB3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM179. Heat Shock Transcription Factor 4 (HSF4, Accession XM\_007871) is another VGAM1936 host target gene. HSF4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSF4 BINDING SITE, designated SEQ ID:30067, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65415] Another function of VGAM1936 is therefore inhibition of Heat Shock Transcription Factor 4 (HSF4, Accession XM\_007871), a gene which activates heat-shock response genes under conditions of heat or other stresses. It was found that HSF4 bound specifically to the heat-shock response element but repressed, rather than activated, transcription. Accordingly, utilities of VGAM1936 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with HSF4. The function of HSF4 has been established by previous studies. Congenital cataracts cause 10 to 30% of all blindness in children, with one-third of cases estimated to have a genetic cause. Lamellar cataract (OMIM Ref. No. 116800) is the most common type of infantile cataract. Bu et al. (2002) carried out whole-genome linkage analysis of Chinese individuals with lamellar cataract, and found that the disorder is associated with inheritance of a 5.11-cM region on chromosome 16. This locus coincides with one previously described for Marner cataract (see OMIM Ref. No. 116800) by Eiberg et al. (1988). Bu et al. (2002) screened individuals of 3 Chinese families for mutations in HSF4 (a gene that maps to this locus) and discovered that in each family, a distinct missense mutation, predicted to affect the DNA-binding domain of the protein, segregated with the disorder. They also discovered an association between a missense mutation and Marner cataract in an extensive Danish family. Thus it appears that HSF4 is critical to lens development. Heat-shock transcription factors (HSFs) activate heat-shock response genes under conditions of heat or other stresses. Other members of the HSF family in-

clude HSF1 (OMIM Ref. No. 140580) and HSF2 (OMIM Ref. No. 140581). Using chicken HSF3 as a probe to screen a human HeLa cDNA library, Nakai et al. (1997) isolated an additional family member, termed HSF4 by the authors. Based on the low level of amino acid identity between chicken HSF3 and HSF4, Nakai et al. (1997) concluded that HSF4 is a novel member of the HSF family, rather than the human homolog of chicken HSF3. They reported that the HSF4 sequence encodes a 463–amino acid polypeptide. Northern blotting revealed that HSF4 is expressed as a 2.5–kb mRNA in the heart, skeletal muscle, and brain, and at much lower levels in some other tissues. Nakai et al. (1997) found that HSF4 bound specifically to the heat–shock response element but repressed, rather than activated, transcription

[65416] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[65417] Bu, L.; Jin, Y.; Shi, Y.; Chu, R.; Ban, A.; Eiberg, H.; Andres, L.; Jiang, H.; Zheng, G.; Qian, M.; Cui, B.; Xia, Y.; Liu, J.; Hu, L.; Zhao, G.; Hayden, M. R.; Kong, X. : Mutant DNA–binding domain of HSF4 is associated with autosomal dominant lamellar and Marner cataract. *Nature Genet.* 31:

276–278, 2002. ; and

[65418] Nakai, A.; Tanabe, M.; Kawazoe, Y.; Inazawa, J.; Morimoto, R. I.; Nagata, K. : HSF4, a new member of the human heat shock factor family which lacks properties of a transcriptional activator.

[65419] Further studies establishing the function and utilities of HSF4 are found in John Hopkins OMIM database record ID 602438, and in cited publications numbered 2022–202 and 5609 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 17 (sodium-dependent inorganic phosphate cotransporter), Member 7 (SLC17A7, Accession NM\_020309) is another VGAM1936 host target gene. SLC17A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC17A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC17A7 BINDING SITE, designated SEQ ID:21557, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65420] Another function of VGAM1936 is therefore inhibition of

Solute Carrier Family 17 (sodium-dependent inorganic phosphate cotransporter), Member 7 (SLC17A7, Accession NM\_020309), a gene which is a brain-specific Na-dependent inorganic phosphate cotransporter. Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC17A7. The function of SLC17A7 has been established by previous studies. Bellocchio et al. (2000) demonstrated that BNPI transports glutamate into synaptic vesicles. In addition, they showed that this vesicular glutamate transporter, which they renamed VGLUT1, exhibits a conductance for chloride that is blocked by glutamate. Bellocchio et al. (2000) found that glutamate was transported by BNPI in the absence of sodium. Vesicular glutamate transport has a substantially lower apparent affinity than the plasma membrane excitatory amino acid transporters. Glutamate transport by BNPI is saturated with a  $K(m)$  of approximately 2 mM, in the same range as transport by synaptic vesicles. Finally, plasma membrane glutamate transporters recognize both aspartate and glutamate as substrates, whereas vesicular glutamate transport does not recognize aspartate. Vesicular glutamate transport has a biphasic dependence on chloride concentration



that may reflect the presence of anion binding site distinct from the site of substrate recognition. Chloride concentrations of approximately 4 to 10 mM appear optimal for transport, with substantially lower activity detected at higher and lower levels. BNPI transports glutamate with all of the functional characteristics previously reported for glutamate transport into native synaptic vesicles from the brain. It localizes to synaptic vesicles, and the mutant *C. elegans eat-4* (a BNPI ortholog) reduces glutamate release. BNPI thus functions as a vesicular glutamate transporter, VGLUT1. Only a subset of glutamate neurons expresses VGLUT1, but a closely related sequence has been identified that appears to be expressed in brain regions that lack VGLUT1 (Aihara et al., 2000). The 2 isoforms together may therefore account for the uptake of glutamate by synaptic vesicles from all glutamatergic neurons. VGLUT1 (BNPI1) may thus function as both a phosphate transporter, presumably at the plasma membrane, and a glutamate transporter in synaptic vesicles. Bellocchio et al. (2000) stated that the localization of VGLUT1 to synaptic vesicles, the phenotype of the *eat-4* mutant, and biochemical evidence strongly suggest that vesicular glutamate transport is its primary role. Takamori et al. (2000)

independently showed that expression of BNPI results in glutamate uptake by intracellular vesicles. Substrate specificity and energy dependence are very similar to glutamate uptake by synaptic vesicles. Stimulation of exocytosis resulted in quantal release of glutamate from BNPI-expressing cells. Furthermore, Takamori et al. (2000) expressed BNPI in neurons containing GABA (see OMIM Ref. No. 137150) and maintained them as cultures of single neurons that form synapses to themselves. After stimulation of these neurons, a component of the postsynaptic current is mediated by glutamate as it is blocked by a combination of the glutamate receptor antagonists, but is insensitive to a GABA-A receptor (see OMIM Ref. No. 137192) antagonist. Takamori et al. (2000) concluded that BNPI functions as a vesicular glutamate transporter and that expression of BNPI suffices to define a glutamatergic phenotype in neurons.

[65421] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[65422] Bellocchio, E. E.; Reimer, R. J.; Fremeau, R. T., Jr.; Edwards, R. H. : Uptake of glutamate into synaptic vesicles by an inorganic phosphate transporter. *Science* 289: 957–960,

2000. ; and

[65423] Takamori, S.; Rhee, J. S.; Rosenmund, C.; Jahn, R. : Identification of a vesicular glutamate transporter that defines a glutamatergic phenotype in neurons. *Nature* 407: 189–194, 2000.

[65424] Further studies establishing the function and utilities of SLC17A7 are found in John Hopkins OMIM database record ID 605208, and in cited publications numbered 6815–6818 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 5 (SLC7A5, Accession NM\_003486) is another VGAM1936 host target gene. SLC7A5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A5 BINDING SITE, designated SEQ ID:9577, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65425] Another function of VGAM1936 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter,

y+ system), Member 5 (SLC7A5, Accession NM\_003486), a gene which mediates transport of large and small neutral amino acids. Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A5. The function of SLC7A5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430. Cell Division Cycle Associated 4 (CDCA4, Accession NM\_017955) is another VGAM1936 host target gene. CDCA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDCA4 BINDING SITE, designated SEQ ID:19662, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65426] Another function of VGAM1936 is therefore inhibition of Cell Division Cycle Associated 4 (CDCA4, Accession NM\_017955). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with CDCA4. CTP Synthase II (CTPS2, Accession NM\_019857) is another VGAM1936 host target gene. CTPS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTPS2 BINDING SITE, designated SEQ ID:21263, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65427] Another function of VGAM1936 is therefore inhibition of CTP Synthase II (CTPS2, Accession NM\_019857). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTPS2. dj309H15.1 (Accession NM\_138574) is another VGAM1936 host target gene. dj309H15.1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by dj309H15.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of dj309H15.1 BINDING SITE, designated SEQ ID:28887, to

the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65428] Another function of VGAM1936 is therefore inhibition of dj309H15.1 (Accession NM\_138574). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with dj309H15.1. DKFZP434C171 (Accession NM\_015621) is another VGAM1936 host target gene. DKFZP434C171 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434C171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C171 BINDING SITE, designated SEQ ID:17884, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65429] Another function of VGAM1936 is therefore inhibition of DKFZP434C171 (Accession NM\_015621). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C171. DKFZP727C091 (Accession XM\_038689) is another VGAM1936 host target gene. DK-

FZP727C091 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP727C091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP727C091 BINDING SITE, designated SEQ ID:32903, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65430] Another function of VGAM1936 is therefore inhibition of DKFZP727C091 (Accession XM\_038689). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP727C091. HSA243666 (Accession NM\_017582) is another VGAM1936 host target gene. HSA243666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA243666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA243666 BINDING SITE, designated SEQ ID:19020, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ

ID:4647.

[65431] Another function of VGAM1936 is therefore inhibition of HSA243666 (Accession NM\_017582). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA243666. KIAA0237 (Accession NM\_014747) is another VGAM1936 host target gene. KIAA0237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16446, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65432] Another function of VGAM1936 is therefore inhibition of KIAA0237 (Accession NM\_014747). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. KIAA0953 (Accession XM\_039733) is another VGAM1936 host target gene. KIAA0953 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0953, corresponding to



a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0953 BINDING SITE, designated SEQ ID:33167, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65433] Another function of VGAM1936 is therefore inhibition of KIAA0953 (Accession XM\_039733). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0953. KIAA1191 (Accession NM\_020444) is another VGAM1936 host target gene. KIAA1191 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1191 BINDING SITE, designated SEQ ID:21685, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65434] Another function of VGAM1936 is therefore inhibition of KIAA1191 (Accession NM\_020444). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1191. KIAA1719 (Accession XM\_042936) is another VGAM1936 host target gene. KIAA1719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33824, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65435] Another function of VGAM1936 is therefore inhibition of KIAA1719 (Accession XM\_042936). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. KIAA1853 (Accession XM\_045184) is another VGAM1936 host target gene. KIAA1853 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1853 BINDING SITE, designated SEQ ID:34388, to the

nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65436] Another function of VGAM1936 is therefore inhibition of KIAA1853 (Accession XM\_045184). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1853. KIAA1922 (Accession XM\_057040) is another VGAM1936 host target gene. KIAA1922 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1922 BINDING SITE, designated SEQ ID:36454, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65437] Another function of VGAM1936 is therefore inhibition of KIAA1922 (Accession XM\_057040). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1922. Retinoic Acid Induced 17 (RAI17, Accession XM\_166091) is another VGAM1936 host target gene. RAI17 BINDING SITE is HOST TARGET binding site found in

the 3` untranslated region of mRNA encoded by RAI17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI17 BINDING SITE, designated SEQ ID:43860, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65438] Another function of VGAM1936 is therefore inhibition of Retinoic Acid Induced 17 (RAI17, Accession XM\_166091). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI17. SCYA5 (Accession NM\_002985) is another VGAM1936 host target gene. SCYA5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SCYA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYA5 BINDING SITE, designated SEQ ID:8882, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65439] Another function of VGAM1936 is therefore inhibition of SCYA5 (Accession NM\_002985). Accordingly, utilities of

VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCYA5. Serine Threonine Kinase 39 (STE20/SPS1 homolog, yeast) (STK39, Accession NM\_013233) is another VGAM1936 host target gene. STK39 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STK39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK39 BINDING SITE, designated SEQ ID:14893, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65440] Another function of VGAM1936 is therefore inhibition of Serine Threonine Kinase 39 (STE20/SPS1 homolog, yeast) (STK39, Accession NM\_013233). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK39. TGFB1-induced Anti-apoptotic Factor 1 (TIAF1, Accession NM\_078471) is another VGAM1936 host target gene. TIAF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TIAF1, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIAF1 BINDING SITE, designated SEQ ID:27799, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65441] Another function of VGAM1936 is therefore inhibition of TGFBI-induced Anti-apoptotic Factor 1 (TIAF1, Accession NM\_078471). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIAF1. LOC113763 (Accession NM\_138434) is another VGAM1936 host target gene. LOC113763 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC113763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113763 BINDING SITE, designated SEQ ID:28799, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65442] Another function of VGAM1936 is therefore inhibition of LOC113763 (Accession NM\_138434). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC113763. LOC138389 (Accession XM\_072534) is another VGAM1936 host target gene. LOC138389 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC138389, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138389 BINDING SITE, designated SEQ ID:37505, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65443] Another function of VGAM1936 is therefore inhibition of LOC138389 (Accession XM\_072534). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138389. LOC144465 (Accession XM\_084874) is another VGAM1936 host target gene. LOC144465 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144465 BINDING SITE, designated SEQ ID:37752, to

the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65444] Another function of VGAM1936 is therefore inhibition of LOC144465 (Accession XM\_084874). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144465. LOC146346 (Accession XM\_085430) is another VGAM1936 host target gene. LOC146346 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146346 BINDING SITE, designated SEQ ID:38138, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65445] Another function of VGAM1936 is therefore inhibition of LOC146346 (Accession XM\_085430). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146346. LOC151176 (Accession XM\_098016) is another VGAM1936 host target gene. LOC151176 BINDING SITE is HOST TARGET binding site found in the 3` un-



translated region of mRNA encoded by LOC151176, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151176 BINDING SITE, designated SEQ ID:41316, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65446] Another function of VGAM1936 is therefore inhibition of LOC151176 (Accession XM\_098016). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151176. LOC163782 (Accession XM\_089138) is another VGAM1936 host target gene. LOC163782 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC163782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163782 BINDING SITE, designated SEQ ID:39963, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65447] Another function of VGAM1936 is therefore inhibition of LOC163782 (Accession XM\_089138). Accordingly, utilities

of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163782. LOC200953 (Accession XM\_117302) is another VGAM1936 host target gene. LOC200953 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC200953, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200953 BINDING SITE, designated SEQ ID:43369, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65448] Another function of VGAM1936 is therefore inhibition of LOC200953 (Accession XM\_117302). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200953. LOC220846 (Accession XM\_165515) is another VGAM1936 host target gene. LOC220846 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC220846, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC220846 BINDING SITE, designated SEQ ID:43664, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65449] Another function of VGAM1936 is therefore inhibition of LOC220846 (Accession XM\_165515). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220846. LOC257000 (Accession XM\_172999) is another VGAM1936 host target gene. LOC257000 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257000, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257000 BINDING SITE, designated SEQ ID:46274, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65450] Another function of VGAM1936 is therefore inhibition of LOC257000 (Accession XM\_172999). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257000. LOC92080 (Accession XM\_042704) is another VGAM1936 host target gene. LOC92080 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92080, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92080 BINDING SITE, designated SEQ ID:33755, to the nucleotide sequence of VGAM1936 RNA, herein designated VGAM RNA, also designated SEQ ID:4647.

[65451] Another function of VGAM1936 is therefore inhibition of LOC92080 (Accession XM\_042704). Accordingly, utilities of VGAM1936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92080. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1937 (VGAM1937) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65452] VGAM1937 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1937 was detected is described hereinabove with reference to Figs. 1–8.

[65453] VGAM1937 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM1937 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65454] VGAM1937 gene encodes a VGAM1937 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1937 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1937 precursor RNA is designated SEQ ID:1923, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1923 is located at position 161986 relative to the genome of Human Herpesvirus 4.

[65455] VGAM1937 precursor RNA folds onto itself, forming VGAM1937 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[65456] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1937 folded precursor RNA into VGAM1937 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1937 RNA is designated SEQ ID:4648, and is provided hereinbelow with reference to the sequence listing part.

[65457] VGAM1937 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1937 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1937 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65458] VGAM1937 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1937 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1937 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1937 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1937 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65459] The complementary binding of VGAM1937 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1937 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1937 host target RNA into VGAM1937 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65460] It is appreciated that VGAM1937 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1937 host target genes. The mRNA of each one of this plurality of VGAM1937 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1937 RNA, herein designated VGAM RNA, and which when bound by VGAM1937 RNA causes inhibition of translation of respective one or more VGAM1937 host target proteins.

[65461] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1937 gene, herein designated VGAM GENE, on one or more VGAM1937 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated



only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65462] It is yet further appreciated that a function of VGAM1937 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1937 correlate with, and may be deduced from, the identity of the host target genes which VGAM1937 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65463] Nucleotide sequences of the VGAM1937 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1937 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1937 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1937 are further described hereinbelow with reference to Table 1.

[65464] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1937 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1937 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65465] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1937 gene, herein designated VGAM is inhibition of expression of VGAM1937 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1937 correlate with, and may be deduced from, the identity of the target genes which VGAM1937 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65466] RAN Binding Protein 3 (RANBP3, Accession NM\_007321) is a VGAM1937 host target gene. RANBP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RANBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of RANBP3 BINDING SITE, designated SEQ ID:14238, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65467] A function of VGAM1937 is therefore inhibition of RAN Binding Protein 3 (RANBP3, Accession NM\_007321). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RANBP3. TIM3 (Accession NM\_032782) is another VGAM1937 host target gene. TIM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIM3 BINDING SITE, designated SEQ ID:26523, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65468] Another function of VGAM1937 is therefore inhibition of TIM3 (Accession NM\_032782), a gene which regulates macrophage activation and enhances the severity of experimental autoimmune encephalomyelitis in mice. Accordingly, utilities of VGAM1937 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with TIM3. The function of TIM3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM909. ALK7 (Accession XM\_065712) is another VGAM1937 host target gene. ALK7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ALK7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALK7 BINDING SITE, designated SEQ ID:37295, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65469] Another function of VGAM1937 is therefore inhibition of ALK7 (Accession XM\_065712). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALK7. C3F (Accession NM\_005768) is another VGAM1937 host target gene. C3F BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C3F, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of C3F BINDING SITE, designated SEQ ID:12332, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65470] Another function of VGAM1937 is therefore inhibition of C3F (Accession NM\_005768). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C3F. DKFZP434N014 (Accession XM\_027012) is another VGAM1937 host target gene. DKFZP434N014 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434N014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434N014 BINDING SITE, designated SEQ ID:30390, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65471] Another function of VGAM1937 is therefore inhibition of DKFZP434N014 (Accession XM\_027012). Accordingly, utilities of VGAM1937 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP434N014. FLJ11565 (Accession NM\_024657) is another VGAM1937 host target gene. FLJ11565 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11565 BINDING SITE, designated SEQ ID:23961, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65472] Another function of VGAM1937 is therefore inhibition of FLJ11565 (Accession NM\_024657). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11565. FLJ14775 (Accession NM\_032837) is another VGAM1937 host target gene. FLJ14775 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14775, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14775 BINDING SITE, designated SEQ ID:26618, to the nucleotide

sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65473] Another function of VGAM1937 is therefore inhibition of FLJ14775 (Accession NM\_032837). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14775. FLJ20174 (Accession NM\_017699) is another VGAM1937 host target gene. FLJ20174 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20174 BINDING SITE, designated SEQ ID:19271, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65474] Another function of VGAM1937 is therefore inhibition of FLJ20174 (Accession NM\_017699). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20174. KIAA0620 (Accession XM\_030707) is another VGAM1937 host target gene. KIAA0620 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0620 BINDING SITE, designated SEQ ID:31124, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65475] Another function of VGAM1937 is therefore inhibition of KIAA0620 (Accession XM\_030707). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0620. Mitogen-activated Protein Kinase Kinase Kinase 2 (MAP3K2, Accession NM\_006609) is another VGAM1937 host target gene. MAP3K2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K2 BINDING SITE, designated SEQ ID:13388, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65476] Another function of VGAM1937 is therefore inhibition of



Mitogen-activated Protein Kinase Kinase Kinase 2 (MAP3K2, Accession NM\_006609). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K2. Neurexophilin 3 (NXPH3, Accession XM\_037847) is another VGAM1937 host target gene. NXPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXPH3 BINDING SITE, designated SEQ ID:32719, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65477] Another function of VGAM1937 is therefore inhibition of Neurexophilin 3 (NXPH3, Accession XM\_037847). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXPH3. START Domain Containing 7 (STARD7, Accession NM\_020151) is another VGAM1937 host target gene. STARD7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STARD7, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STARD7 BINDING SITE, designated SEQ ID:21356, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65478] Another function of VGAM1937 is therefore inhibition of START Domain Containing 7 (STARD7, Accession NM\_020151). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STARD7. Three Prime Repair Exonuclease 1 (TREX1, Accession NM\_016381) is another VGAM1937 host target gene. TREX1 BINDING SITE1 through TREX1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TREX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TREX1 BINDING SITE1 through TREX1 BINDING SITE3, designated SEQ ID:18520, SEQ ID:27345 and SEQ ID:27336 respectively, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65479] Another function of VGAM1937 is therefore inhibition of Three Prime Repair Exonuclease 1 (TREX1, Accession NM\_016381). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TREX1. LOC149373 (Accession XM\_086507) is another VGAM1937 host target gene. LOC149373 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149373 BINDING SITE, designated SEQ ID:38720, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65480] Another function of VGAM1937 is therefore inhibition of LOC149373 (Accession XM\_086507). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149373. LOC149668 (Accession XM\_097692) is another VGAM1937 host target gene. LOC149668 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149668, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149668 BINDING SITE, designated SEQ ID:41031, to the nucleotide sequence of VGAM1937 RNA, herein designated VGAM RNA, also designated SEQ ID:4648.

[65481] Another function of VGAM1937 is therefore inhibition of LOC149668 (Accession XM\_097692). Accordingly, utilities of VGAM1937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149668. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1938 (VGAM1938) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65482] VGAM1938 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1938 was detected is described hereinabove with reference to Figs. 1-8.

[65483] VGAM1938 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4.

VGAM1938 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65484] VGAM1938 gene encodes a VGAM1938 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1938 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1938 precursor RNA is designated SEQ ID:1924, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1924 is located at position 151796 relative to the genome of Human Herpesvirus 4.

[65485] VGAM1938 precursor RNA folds onto itself, forming VGAM1938 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65486] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1938 folded precursor RNA into VGAM1938 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1938 RNA is designated SEQ ID:4649, and is provided hereinbelow with reference to the sequence listing part.

[65487] VGAM1938 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1938 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1938 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65488] VGAM1938 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1938 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1938 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1938 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1938 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65489] The complementary binding of VGAM1938 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1938 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1938 host target RNA into VGAM1938 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65490] It is appreciated that VGAM1938 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1938 host target genes. The mRNA of each one of this plurality of VGAM1938 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1938 RNA, herein designated VGAM RNA, and which when bound by VGAM1938 RNA causes inhibition of translation of respective one or more VGAM1938 host target proteins.

[65491] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1938 gene, herein designated VGAM GENE, on one or more VGAM1938 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65492] It is yet further appreciated that a function of VGAM1938 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1938 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1938 correlate with, and may be deduced from, the identity of the host target genes which VGAM1938 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65493] Nucleotide sequences of the VGAM1938 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1938 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1938 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1938 are further described hereinbelow with reference to Table 1.

[65494] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1938 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1938 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65495] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1938 gene, herein designated VGAM is inhibition of expression of VGAM1938 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1938 correlate with, and may be deduced from, the identity of the target genes which VGAM1938 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65496] Cyclin-dependent Kinase 2 (CDK2, Accession NM\_001798) is a VGAM1938 host target gene. CDK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK2 BINDING SITE, designated SEQ ID:7553, to the nucleotide se-

quence of VGAM1938 RNA, herein designated VGAM RNA, also designated SEQ ID:4649.

[65497] A function of VGAM1938 is therefore inhibition of Cyclin-dependent Kinase 2 (CDK2, Accession NM\_001798), a gene which plays a unique role in cell cycle regulation of vertebrate cells. Accordingly, utilities of VGAM1938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK2. The function of CDK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1467. Zinc Finger Protein 83 (HPF1) (ZNF83, Accession NM\_018300) is another VGAM1938 host target gene. ZNF83 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF83, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF83 BINDING SITE, designated SEQ ID:20293, to the nucleotide sequence of VGAM1938 RNA, herein designated VGAM RNA, also designated SEQ ID:4649.

[65498] Another function of VGAM1938 is therefore inhibition of Zinc Finger Protein 83 (HPF1) (ZNF83, Accession

NM\_018300). Accordingly, utilities of VGAM1938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF83. Baculoviral IAP Repeat-containing 1 (BIRC1, Accession NM\_004536) is another VGAM1938 host target gene. BIRC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BIRC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIRC1 BINDING SITE, designated SEQ ID:10881, to the nucleotide sequence of VGAM1938 RNA, herein designated VGAM RNA, also designated SEQ ID:4649.

[65499] Another function of VGAM1938 is therefore inhibition of Baculoviral IAP Repeat-containing 1 (BIRC1, Accession NM\_004536). Accordingly, utilities of VGAM1938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC1. FLJ20651 (Accession NM\_017919) is another VGAM1938 host target gene. FLJ20651 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20651, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20651 BINDING SITE, designated SEQ ID:19574, to the nucleotide sequence of VGAM1938 RNA, herein designated VGAM RNA, also designated SEQ ID:4649.

[65500] Another function of VGAM1938 is therefore inhibition of FLJ20651 (Accession NM\_017919). Accordingly, utilities of VGAM1938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20651. KIAA0391 (Accession NM\_014672) is another VGAM1938 host target gene. KIAA0391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0391 BINDING SITE, designated SEQ ID:16140, to the nucleotide sequence of VGAM1938 RNA, herein designated VGAM RNA, also designated SEQ ID:4649.

[65501] Another function of VGAM1938 is therefore inhibition of KIAA0391 (Accession NM\_014672). Accordingly, utilities of VGAM1938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0391. LATS, Large Tumor Suppressor, Homolog 1 (Drosophila) (LATS1, Accession XM\_015547) is another VGAM1938 host target gene. LATS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LATS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LATS1 BINDING SITE, designated SEQ ID:30238, to the nucleotide sequence of VGAM1938 RNA, herein designated VGAM RNA, also designated SEQ ID:4649.

[65502] Another function of VGAM1938 is therefore inhibition of LATS, Large Tumor Suppressor, Homolog 1 (Drosophila) (LATS1, Accession XM\_015547). Accordingly, utilities of VGAM1938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LATS1. MGC2452 (Accession NM\_032644) is another VGAM1938 host target gene. MGC2452 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC2452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2452 BINDING SITE,

designated SEQ ID:26375, to the nucleotide sequence of VGAM1938 RNA, herein designated VGAM RNA, also designated SEQ ID:4649.

[65503] Another function of VGAM1938 is therefore inhibition of MGC2452 (Accession NM\_032644). Accordingly, utilities of VGAM1938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2452. LOC144473 (Accession XM\_096606) is another VGAM1938 host target gene. LOC144473 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144473, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144473 BINDING SITE, designated SEQ ID:40414, to the nucleotide sequence of VGAM1938 RNA, herein designated VGAM RNA, also designated SEQ ID:4649.

[65504] Another function of VGAM1938 is therefore inhibition of LOC144473 (Accession XM\_096606). Accordingly, utilities of VGAM1938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144473. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1939 (VGAM1939) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65505] VGAM1939 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1939 was detected is described hereinabove with reference to Figs. 1–8.

[65506] VGAM1939 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Measles Virus. VGAM1939 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65507] VGAM1939 gene encodes a VGAM1939 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1939 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1939 precursor RNA is designated SEQ ID:1925, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1925 is located at position 15073 relative to the



genome of Measles Virus.

[65508] VGAM1939 precursor RNA folds onto itself, forming VGAM1939 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65509] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1939 folded precursor RNA into VGAM1939 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1939 RNA is designated SEQ ID:4650, and is provided hereinbelow with reference to the sequence listing part.

[65510] VGAM1939 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1939 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1939 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[65511] VGAM1939 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1939 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1939 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1939 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1939 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65512] The complementary binding of VGAM1939 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1939 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1939 host target RNA into VGAM1939 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65513] It is appreciated that VGAM1939 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1939 host target genes. The mRNA of each one of this plurality of VGAM1939 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1939 RNA, herein designated VGAM RNA, and which when bound by VGAM1939 RNA causes inhibition of translation of respective one or more VGAM1939 host target proteins.

[65514] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1939 gene, herein designated VGAM GENE, on one or more VGAM1939 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65515] It is yet further appreciated that a function of VGAM1939 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1939 include diagnosis, prevention and treatment of viral infection by Measles Virus. Specific functions, and accordingly utilities, of VGAM1939 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1939 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65516] Nucleotide sequences of the VGAM1939 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1939 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1939 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1939 are further described hereinbelow with reference to Table 1.

[65517] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1939 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1939 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65518] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1939 gene, herein designated VGAM is inhibition of expression of VGAM1939 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1939 correlate with, and may be deduced

from, the identity of the target genes which VGAM1939 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65519] Potassium Voltage-gated Channel, Shal-related Subfamily, Member 1 (KCND1, Accession NM\_004979) is a VGAM1939 host target gene. KCND1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCND1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCND1 BINDING SITE, designated SEQ ID:11423, to the nucleotide sequence of VGAM1939 RNA, herein designated VGAM RNA, also designated SEQ ID:4650.

[65520] A function of VGAM1939 is therefore inhibition of Potassium Voltage-gated Channel, Shal-related Subfamily, Member 1 (KCND1, Accession NM\_004979). Accordingly, utilities of VGAM1939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCND1. LOC122553 (Accession XM\_058630) is another VGAM1939 host target gene. LOC122553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122553, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122553 BINDING SITE, designated SEQ ID:36686, to the nucleotide sequence of VGAM1939 RNA, herein designated VGAM RNA, also designated SEQ ID:4650.

[65521] Another function of VGAM1939 is therefore inhibition of LOC122553 (Accession XM\_058630). Accordingly, utilities of VGAM1939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122553. LOC157869 (Accession XM\_088409) is another VGAM1939 host target gene. LOC157869 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157869, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157869 BINDING SITE, designated SEQ ID:39676, to the nucleotide sequence of VGAM1939 RNA, herein designated VGAM RNA, also designated SEQ ID:4650.

[65522] Another function of VGAM1939 is therefore inhibition of LOC157869 (Accession XM\_088409). Accordingly, utilities of VGAM1939 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC157869. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1940 (VGAM1940) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65523] VGAM1940 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1940 was detected is described hereinabove with reference to Figs. 1–8.

[65524] VGAM1940 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1940 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65525] VGAM1940 gene encodes a VGAM1940 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1940 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1940 precursor RNA is desig-



nated SEQ ID:1926, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1926 is located at position 17783 relative to the genome of Variola Virus.

- [65526] VGAM1940 precursor RNA folds onto itself, forming VGAM1940 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [65527] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1940 folded precursor RNA into VGAM1940 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM1940 RNA is designated SEQ ID:4651, and is provided hereinbelow with reference to the sequence

listing part.

[65528] VGAM1940 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1940 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1940 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65529] VGAM1940 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1940 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1940 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1940 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1940 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65530] The complementary binding of VGAM1940 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1940 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1940 host target RNA into VGAM1940 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65531] It is appreciated that VGAM1940 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1940 host target genes. The mRNA of each one of this plurality of VGAM1940 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1940 RNA, herein designated VGAM

RNA, and which when bound by VGAM1940 RNA causes inhibition of translation of respective one or more VGAM1940 host target proteins.

[65532] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1940 gene, herein designated VGAM GENE, on one or more VGAM1940 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65533] It is yet further appreciated that a function of VGAM1940 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1940 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1940 correlate with, and may be deduced from, the identity of the host target genes which VGAM1940 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65534] Nucleotide sequences of the VGAM1940 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1940 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1940 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1940 are further described hereinbelow with reference to Table 1.

[65535] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1940 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1940 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65536] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1940 gene, herein designated VGAM is

inhibition of expression of VGAM1940 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1940 correlate with, and may be deduced from, the identity of the target genes which VGAM1940 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65537] C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252) is a VGAM1940 host target gene. CLECSF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLECSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF5 BINDING SITE, designated SEQ ID:14923, to the nucleotide sequence of VGAM1940 RNA, herein designated VGAM RNA, also designated SEQ ID:4651.

[65538] A function of VGAM1940 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252). Accordingly, utilities of VGAM1940 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with CLECSF5. Interleukin 21 Receptor (IL21R, Accession NM\_021798) is another VGAM1940 host target gene. IL21R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL21R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL21R BINDING SITE, designated SEQ ID:22354, to the nucleotide sequence of VGAM1940 RNA, herein designated VGAM RNA, also designated SEQ ID:4651.

[65539] Another function of VGAM1940 is therefore inhibition of Interleukin 21 Receptor (IL21R, Accession NM\_021798), a gene which is involved in receptor mediated endocytosis and transduces the mitogenic signals of il-2. Accordingly, utilities of VGAM1940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL21R. The function of IL21R has been established by previous studies. Type I cytokine receptors include receptors for hematopoietic growth factors as well as for many of the interleukins (e.g., IL2; 147680). Some type I receptors are capable of signaling through homodimerization. Others share a common beta chain or the common cy-

tokine receptor gamma chain, gamma(c) (IL2RG; 308380), mutation of which results in X-linked severe combined immunodeficiency (300400 Ueda et al. (2002) found that the IL21R gene is the partner of BCL6 (OMIM Ref. No. 109565) in the t(3;16)(q27;p11) translocation. In 2 cases they found that the breakpoints on 16p11 were located within the 27-kb intron 1 of IL21R. As a result of t(3;16), the promoter region of IL21R was substituted for the regulatory sequences of BCL6 in the same transcriptional orientation. Fluorescence in situ chromosomal hybridization of lymphoma metaphase cells revealed fusion signals that contained both the BCL6 and IL21R sequences on the der(3)t(3;16) chromosome. To the list of nonimmunoglobulin partners of BCL6 translocations, this study added a new class of gene, i.e., cytokine receptor gene, the expression of which is closely associated with lymphoid cells. Animal model experiments lend further support to the function of IL21R. Kasaian et al. (2002) generated IL21r-deficient mice by homologous recombination and deletion of exon 1. The mice had normal NK cell development and responses to poly I:C in vivo or IL15 in vitro, but not to IL21. In wildtype mice, IL21 limited the growth but not activation of NK cells, but not T cells, in response to



IL15 or IL2 in antigen-free cultures. IL21 could boost the function of activated NK cells from these mice without promoting NK cell viability or preventing apoptosis. CD8 (see OMIM Ref. No. 186910)-positive T cells from either wildtype or Il21r -/- mice treated with IL15 proliferated and expressed high levels of CD44 (OMIM Ref. No. 107269), a marker for 'memory' T cells. Addition of IL21 counteracted the effects of IL15 in wildtype but not Il21r-deficient mice and also prevented the expansion of cells expressing the gamma-interferon (IFNG; 147570) receptor, CD119 (IFNGR1; 107470), as well as those expressing IL2RA (CD25; 147730) and IL2RB/IL15RB (CD122), but not IL2RG (CD132). IL21 enhanced proliferation and effector functions of wildtype cytolytic T cells stimulated with either anti-CD3 (see OMIM Ref. No. 186830) or allogeneic cells. Kasaian et al. (2002) proposed that IL21 promotes the transition between innate and adaptive immunity.

[65540] It is appreciated that the abovementioned animal model for IL21R is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[65541] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [65542] Ueda, C.; Akasaka, T.; Kurata, M.; Maesako, Y.; Nishikori, M.; Ichinohasama, R.; Imada, K.; Uchiyama, T.; Ohno, H. : The gene for interleukin-21 receptor is the partner of BCL6 in t(13;16)(q27;p11), which is recurrently observed in diffuse large B-cell lymphoma. *Oncogene* 21: 368-376, 2002. ; and
- [65543] Kasaian, M. T.; Whitters, M. J.; Carter, L. L.; Lowe, L. D.; Jussif, J. M.; Deng, B.; Johnson, K. A.; Witek, J. S.; Senices, M.; Konz, R. F.; Wurster, A. L.; Donaldson, D. D.; Collins.
- [65544] Further studies establishing the function and utilities of IL21R are found in John Hopkins OMIM database record ID 605383, and in cited publications numbered 9015, 4416-441 and 1383 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Keratocan (KERA, Accession NM\_007035) is another VGAM1940 host target gene. KERA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KERA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KERA BINDING SITE,

designated SEQ ID:13910, to the nucleotide sequence of VGAM1940 RNA, herein designated VGAM RNA, also designated SEQ ID:4651.

[65545] Another function of VGAM1940 is therefore inhibition of Keratocan (KERA, Accession NM\_007035), a gene which may be important in developing and maintaining corneal transparency and for the structure of the stromal matrix. Accordingly, utilities of VGAM1940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KERA. The function of KERA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM723.V-yes-1 Yamaguchi Sarcoma Viral Oncogene Homolog 1 (YES1, Accession NM\_005433) is another VGAM1940 host target gene. YES1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YES1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YES1 BINDING SITE, designated SEQ ID:11913, to the nucleotide sequence of VGAM1940 RNA, herein designated VGAM RNA, also designated SEQ ID:4651.

[65546] Another function of VGAM1940 is therefore inhibition of V–yes–1 Yamaguchi Sarcoma Viral Oncogene Homolog 1 (YES1, Accession NM\_005433), a gene which is a putative protein–tyrosine kinase. Accordingly, utilities of VGAM1940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YES1. The function of YES1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.LOC200059 (Accession XM\_114104) is another VGAM1940 host target gene. LOC200059 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC200059, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200059 BINDING SITE, designated SEQ ID:42700, to the nucleotide sequence of VGAM1940 RNA, herein designated VGAM RNA, also designated SEQ ID:4651.

[65547] Another function of VGAM1940 is therefore inhibition of LOC200059 (Accession XM\_114104). Accordingly, utilities of VGAM1940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC200059. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1941 (VGAM1941) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65548] VGAM1941 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1941 was detected is described hereinabove with reference to Figs. 1–8.

[65549] VGAM1941 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1941 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65550] VGAM1941 gene encodes a VGAM1941 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1941 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1941 precursor RNA is designated SEQ ID:1927, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1927 is located at position 17196 relative to the genome of Variola Virus.

- [65551] VGAM1941 precursor RNA folds onto itself, forming VGAM1941 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [65552] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1941 folded precursor RNA into VGAM1941 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1941 RNA is designated SEQ ID:4652, and is provided hereinbelow with reference to the sequence listing part.

[65553] VGAM1941 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1941 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1941 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65554] VGAM1941 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1941 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1941 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1941 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1941 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65555] The complementary binding of VGAM1941 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1941 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1941 host target RNA into VGAM1941 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65556] It is appreciated that VGAM1941 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1941 host target genes. The mRNA of each one of this plurality of VGAM1941 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1941 RNA, herein designated VGAM RNA, and which when bound by VGAM1941 RNA causes



inhibition of translation of respective one or more VGAM1941 host target proteins.

[65557] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1941 gene, herein designated VGAM GENE, on one or more VGAM1941 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65558] It is yet further appreciated that a function of VGAM1941 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1941 include diagnosis, prevention and

treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1941 correlate with, and may be deduced from, the identity of the host target genes which VGAM1941 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65559] Nucleotide sequences of the VGAM1941 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1941 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1941 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1941 are further described hereinbelow with reference to Table 1.

[65560] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1941 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1941 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65561] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1941 gene, herein designated VGAM is inhibition of expression of VGAM1941 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1941 correlate with, and may be deduced from, the identity of the target genes which VGAM1941 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65562] Adenosine Deaminase, TRNA-specific 1 (ADAT1, Accession NM\_012091) is a VGAM1941 host target gene. ADAT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAT1 BINDING SITE, designated SEQ ID:14381, to the nucleotide sequence of VGAM1941 RNA, herein designated VGAM RNA, also designated SEQ ID:4652.

[65563] A function of VGAM1941 is therefore inhibition of Adenosine Deaminase, TRNA-specific 1 (ADAT1, Accession NM\_012091), a gene which TRNA-specific adenosine deaminase; deaminates A(37) in the anticodon loop of tRNA(Ala). Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAT1. The function of ADAT1

has been established by previous studies. The mammalian RNA-specific adenosine deaminases (ADARs; OMIM Ref. No. 601059) constitute a family of sequence-related proteins involved in pre-mRNA editing of nuclear transcripts through site-specific adenosine modification. Maas et al. (1999) identified and characterized a human ADAR-related protein that specifically deaminates adenosine-37 to inosine in eukaryotic tRNA(ala). They designated this predicted 502-amino acid protein 'adenosine deaminase acting on tRNA,' or ADAT1, and concluded that it probably represents the human counterpart of the yeast protein Tad1p. Southern blot analysis revealed that the ADAT1 enzyme is represented by a single gene. Northern blot analysis detected ADAT1 transcripts of approximately 5 and 6.5 kb in all human tissues, with highest expression levels in heart, brain, and pancreas. By radiation hybrid panel analysis, Maas et al. (2001) mapped the ADAT1 gene and the gene encoding lysyl tRNA synthetase (KARS; 601421) to 16q22.2-q22.3, with the gene for alanyl tRNA synthetase (AARS; 601065) positioned centromeric to the KARS and ADAT1 genes. They speculated that the clustering of 3 tRNA-specific genes, of which 2 are specific for tRNA(Ala), may indicate their evolutionary relatedness or

common factors involved in regulating their expression.

[65564] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[65565] Maas, S.; Gerber, A. P.; Rich, A. : Identification and characterization of a human tRNA-specific adenosine deaminase related to the ADAR family of pre-mRNA editing enzymes. Proc. Nat. Acad. Sci. 96: 8895–8900, 1999. ; and

[65566] Maas, S.; Kim, Y.-G.; Rich, A. : Genomic clustering of tRNA-specific adenosine deaminase ADAT1 and two tRNA synthetases. Mammalian Genome 12: 387–393, 2001.

[65567] Further studies establishing the function and utilities of ADAT1 are found in John Hopkins OMIM database record ID 604230, and in cited publications numbered 519 and 7815 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nijmegen Breakage Syndrome 1 (nibrin) (NBS1, Accession XM\_045343) is another VGAM1941 host target gene. NBS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NBS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

NBS1 BINDING SITE, designated SEQ ID:34433, to the nucleotide sequence of VGAM1941 RNA, herein designated VGAM RNA, also designated SEQ ID:4652.

[65568] Another function of VGAM1941 is therefore inhibition of Nijmegen Breakage Syndrome 1 (nibrin) (NBS1, Accession XM\_045343), a gene which may be involved in repair of DNA double-strand breaks. Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBS1. The function of NBS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM450. Nuclear Receptor Coactivator 3 (NCOA3, Accession NM\_006534) is another VGAM1941 host target gene. NCOA3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NCOA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCOA3 BINDING SITE, designated SEQ ID:13285, to the nucleotide sequence of VGAM1941 RNA, herein designated VGAM RNA, also designated SEQ ID:4652.

[65569] Another function of VGAM1941 is therefore inhibition of Nuclear Receptor Coactivator 3 (NCOA3, Accession NM\_006534), a gene which directly binds nuclear receptors and stimulates the transcriptional activities in hormone-dependent fashion. Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCOA3. The function of NCOA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM215. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 2 (PPP1R2, Accession NM\_006241) is another VGAM1941 host target gene. PPP1R2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R2 BINDING SITE, designated SEQ ID:12906, to the nucleotide sequence of VGAM1941 RNA, herein designated VGAM RNA, also designated SEQ ID:4652.

[65570] Another function of VGAM1941 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 2

(PPP1R2, Accession NM\_006241), a gene which suggests a housekeeping promoter structure. Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R2. The function of PPP1R2 has been established by previous studies. Using a cosmid that contained the gene for phospholipase C-beta-3 (PLCB3; 600230), Lagercrantz et al. (1996) isolated and characterized a gene that they called PLCB3-neighboring gene (PNG). PLCB3 is located on 11q13. PNG had no striking similarity to other known genes at the DNA level, however, analysis of hybridization to a panel of somatic cell hybrids indicated the existence of related sequences on chromosomes 2, 4, 7, and 22. PNG showed expression of a 1-kb message in multiple tissues. The predicted protein is 119 amino acids long. The gene spans approximately 2.5 kb and is divided into 4 exons and 3 introns. It is located 4.4 kb upstream of PLCB3, with the 5-prime ends of each gene facing each other. The intragenic region showed separate CpG islands at each end separated by a stretch of 2 kb, characterized by periodic alteration of the GC content. A 5-prime flanking region of PNG did not contain TATA or CCAAT, suggesting to the authors a housekeeping promoter struc-



ture. Lagercrantz et al. (1996) described isolation and expression of the murine homolog. The predicted murine protein contains 203 amino acids

[65571] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[65572] Lagercrantz, J.; Carson, E.; Larsson, C.; Nordenskjold, M.; Weber, G. : Isolation and characterization of a novel gene close to the human phosphoinositide-specific phospholipase C beta-3 gene on chromosomal region 11q13. *Genomics* 31: 380-384, 1996. ; and

[65573] Lagercrantz, J.; Kedra, D.; Carson, E.; Nordenskjold, M.; Dumanski, J. P.; Weber, G.; Piehl, F. : Sequence and expression of the mouse homologue to human phospholipase C beta-3 neighbor.

[65574] Further studies establishing the function and utilities of PPP1R2 are found in John Hopkins OMIM database record ID 601792, and in cited publications numbered 5792-5799 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 10 (sodium/bile acid cotransporter family), Member 2 (SLC10A2, Accession NM\_000452) is another VGAM1941 host target gene. SLC10A2 BINDING SITE1 and

SLC10A2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC10A2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC10A2 BINDING SITE1 and SLC10A2 BINDING SITE2, designated SEQ ID:6062 and SEQ ID:6061 respectively, to the nucleotide sequence of VGAM1941 RNA, herein designated VGAM RNA, also designated SEQ ID:4652.

[65575] Another function of VGAM1941 is therefore inhibition of Solute Carrier Family 10 (sodium/bile acid cotransporter family), Member 2 (SLC10A2, Accession NM\_000452). Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC10A2. Zinc Finger Protein 141 (clone pHZ-44) (ZNF141, Accession NM\_003441) is another VGAM1941 host target gene. ZNF141 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF141, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF141

BINDING SITE, designated SEQ ID:9498, to the nucleotide sequence of VGAM1941 RNA, herein designated VGAM RNA, also designated SEQ ID:4652.

[65576] Another function of VGAM1941 is therefore inhibition of Zinc Finger Protein 141 (clone pHZ-44) (ZNF141, Accession NM\_003441). Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF141. Cellular Repressor of E1A-stimulated Genes (CREG, Accession NM\_003851) is another VGAM1941 host target gene. CREG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CREG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CREG BINDING SITE, designated SEQ ID:9946, to the nucleotide sequence of VGAM1941 RNA, herein designated VGAM RNA, also designated SEQ ID:4652.

[65577] Another function of VGAM1941 is therefore inhibition of Cellular Repressor of E1A-stimulated Genes (CREG, Accession NM\_003851). Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CREG. KIAA0349

(Accession XM\_166449) is another VGAM1941 host target gene. KIAA0349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0349 BINDING SITE, designated SEQ ID:44339, to the nucleotide sequence of VGAM1941 RNA, herein designated VGAM RNA, also designated SEQ ID:4652.

[65578] Another function of VGAM1941 is therefore inhibition of KIAA0349 (Accession XM\_166449). Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0349. LOC153743 (Accession XM\_018216) is another VGAM1941 host target gene. LOC153743 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153743 BINDING SITE, designated SEQ ID:30348, to the nucleotide sequence of VGAM1941 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4652.

[65579] Another function of VGAM1941 is therefore inhibition of LOC153743 (Accession XM\_018216). Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153743. LOC200227 (Accession XM\_114162) is another VGAM1941 host target gene. LOC200227 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200227, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200227 BINDING SITE, designated SEQ ID:42747, to the nucleotide sequence of VGAM1941 RNA, herein designated VGAM RNA, also designated SEQ ID:4652.

[65580] Another function of VGAM1941 is therefore inhibition of LOC200227 (Accession XM\_114162). Accordingly, utilities of VGAM1941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200227. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1942 (VGAM1942) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65581] VGAM1942 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1942 was detected is described hereinabove with reference to Figs. 1–8.

[65582] VGAM1942 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1942 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65583] VGAM1942 gene encodes a VGAM1942 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1942 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1942 precursor RNA is designated SEQ ID:1928, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1928 is located at position 17313 relative to the genome of Variola Virus.

[65584] VGAM1942 precursor RNA folds onto itself, forming

VGAM1942 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65585] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1942 folded precursor RNA into VGAM1942 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1942 RNA is designated SEQ ID:4653, and is provided hereinbelow with reference to the sequence listing part.

[65586] VGAM1942 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1942 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1942 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65587] VGAM1942 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1942 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1942 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1942 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1942 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example



only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65588] The complementary binding of VGAM1942 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1942 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1942 host target RNA into VGAM1942 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65589] It is appreciated that VGAM1942 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1942 host target genes. The mRNA of each one of this plurality of VGAM1942 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1942 RNA, herein designated VGAM RNA, and which when bound by VGAM1942 RNA causes inhibition of translation of respective one or more VGAM1942 host target proteins.

[65590] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1942 gene, herein designated VGAM GENE, on one or more VGAM1942 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65591] It is yet further appreciated that a function of VGAM1942 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1942 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1942 correlate with, and may be deduced from, the identity of the host target genes which VGAM1942 binds and inhibits, and the

function of these host target genes, as elaborated herein–below.

[65592] Nucleotide sequences of the VGAM1942 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1942 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1942 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1942 are further described hereinbelow with reference to Table 1.

[65593] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM1942 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1942 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65594] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1942 gene, herein designated VGAM is inhibition of expression of VGAM1942 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1942 correlate with, and may be deduced from, the identity of the target genes which VGAM1942 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[65595] Cyclin-dependent Kinase Inhibitor 1A (p21, Cip1) (CDKN1A, Accession NM\_078467) is a VGAM1942 host target gene. CDKN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDKN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN1A BINDING SITE, designated SEQ ID:27782, to the nucleotide sequence of VGAM1942 RNA, herein designated VGAM RNA, also designated SEQ ID:4653.

[65596] A function of VGAM1942 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 1A (p21, Cip1) (CDKN1A, Accession NM\_078467), a gene which inhibits cyclin-kinase activity and probably serves as the effector of p53 cell cycle control. Accordingly, utilities of VGAM1942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN1A. The function of CDKN1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1912. Phosphatidylinositol-4-phosphate 5-kinase,

Type I, Gamma (PIP5K1C, Accession XM\_047620) is another VGAM1942 host target gene. PIP5K1C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP5K1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP5K1C BINDING SITE, designated SEQ ID:35014, to the nucleotide sequence of VGAM1942 RNA, herein designated VGAM RNA, also designated SEQ ID:4653.

[65597] Another function of VGAM1942 is therefore inhibition of Phosphatidylinositol-4-phosphate 5-kinase, Type I, Gamma (PIP5K1C, Accession XM\_047620). Accordingly, utilities of VGAM1942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP5K1C. LOC253792 (Accession XM\_173186) is another VGAM1942 host target gene. LOC253792 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253792, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253792 BINDING SITE, designated SEQ ID:46430, to

the nucleotide sequence of VGAM1942 RNA, herein designated VGAM RNA, also designated SEQ ID:4653.

[65598] Another function of VGAM1942 is therefore inhibition of LOC253792 (Accession XM\_173186). Accordingly, utilities of VGAM1942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253792. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1943 (VGAM1943) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65599] VGAM1943 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1943 was detected is described hereinabove with reference to Figs. 1–8.

[65600] VGAM1943 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus.

VGAM1943 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65601] VGAM1943 gene encodes a VGAM1943 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1943 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1943 precursor RNA is designated SEQ ID:1929, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1929 is located at position 6220 relative to the genome of Variola Virus.

[65602] VGAM1943 precursor RNA folds onto itself, forming VGAM1943 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65603] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1943 folded precursor RNA into VGAM1943 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1943 RNA is designated SEQ ID:4654, and is provided hereinbelow with reference to the sequence listing part.

[65604] VGAM1943 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1943 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1943 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65605] VGAM1943 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1943 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1943 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding



sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1943 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1943 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65606] The complementary binding of VGAM1943 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1943 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1943 host target RNA into VGAM1943 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65607] It is appreciated that VGAM1943 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1943 host target genes. The mRNA of each one of this plurality of VGAM1943 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1943 RNA, herein designated VGAM RNA, and which when bound by VGAM1943 RNA causes inhibition of translation of respective one or more VGAM1943 host target proteins.

[65608] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1943 gene, herein designated VGAM GENE, on one or more VGAM1943 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science  
294,779 (2001)).

[65609] It is yet further appreciated that a function of VGAM1943 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1943 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1943 correlate with, and may be deduced from, the identity of the host target genes which VGAM1943 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65610] Nucleotide sequences of the VGAM1943 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1943 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1943 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1943 are further described hereinbelow with reference to Table 1.

[65611] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1943 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1943 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65612] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1943 gene, herein designated VGAM is inhibition of expression of VGAM1943 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1943 correlate with, and may be deduced from, the identity of the target genes which VGAM1943 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65613] Protein Kinase, CAMP-dependent, Regulatory, Type II, Beta (PRKAR2B, Accession NM\_002736) is a VGAM1943 host target gene. PRKAR2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKAR2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAR2B BINDING SITE, designated SEQ ID:8610, to the nucleotide sequence of VGAM1943 RNA, herein designated VGAM RNA, also designated SEQ ID:4654.

[65614] A function of VGAM1943 is therefore inhibition of Protein

Kinase, CAMP-dependent, Regulatory, Type II, Beta (PRKAR2B, Accession NM\_002736), a gene which type ii regulatory chains mediate membrane association by binding to anchoring proteins, including the map2 kinase. Accordingly, utilities of VGAM1943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAR2B. The function of PRKAR2B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1944 (VGAM1944) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65615] VGAM1944 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1944 was detected is described hereinabove with reference to Figs. 1-8.

[65616] VGAM1944 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus.

VGAM1944 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[65617] VGAM1944 gene encodes a VGAM1944 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1944 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1944 precursor RNA is designated SEQ ID:1930, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1930 is located at position 4789 relative to the genome of Variola Virus.

[65618] VGAM1944 precursor RNA folds onto itself, forming VGAM1944 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65619] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1944 folded precursor RNA into VGAM1944

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1944 RNA is designated SEQ ID:4655, and is provided hereinbelow with reference to the sequence listing part.

[65620] VGAM1944 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1944 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1944 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65621] VGAM1944 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1944 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1944 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1944 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1944 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65622] The complementary binding of VGAM1944 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1944 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1944 host target RNA into VGAM1944 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM



host target protein is therefore outlined by a broken line.

[65623] It is appreciated that VGAM1944 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1944 host target genes. The mRNA of each one of this plurality of VGAM1944 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1944 RNA, herein designated VGAM RNA, and which when bound by VGAM1944 RNA causes inhibition of translation of respective one or more VGAM1944 host target proteins.

[65624] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1944 gene, herein designated VGAM GENE, on one or more VGAM1944 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65625] It is yet further appreciated that a function of VGAM1944 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1944 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1944 correlate with, and may be deduced from, the identity of the host target genes which VGAM1944 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65626] Nucleotide sequences of the VGAM1944 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1944 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1944 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1944 are further described hereinbelow with reference to Table 1.

[65627] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1944 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1944 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65628] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1944 gene, herein designated VGAM is inhibition of expression of VGAM1944 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1944 correlate with, and may be deduced from, the identity of the target genes which VGAM1944 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65629] Osteoglycin (osteoinductive factor, mimecan) (OGN, Accession NM\_014057) is a VGAM1944 host target gene. OGN BINDING SITE1 through OGN BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OGN, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OGN BINDING SITE1 through OGN BINDING SITE3, designated SEQ ID:15276,

SEQ ID:23656 and SEQ ID:26900 respectively, to the nucleotide sequence of VGAM1944 RNA, herein designated VGAM RNA, also designated SEQ ID:4655.

[65630] A function of VGAM1944 is therefore inhibition of Osteoglycin (osteoinductive factor, mimecan) (OGN, Accession NM\_014057), a gene which induces ectopic bone formation in conjunction with transforming growth factor beta. Accordingly, utilities of VGAM1944 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OGN. The function of OGN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM346.CCR4-NOT Transcription Complex, Subunit 7 (CNOT7, Accession NM\_013354) is another VGAM1944 host target gene. CNOT7 BINDING SITE1 and CNOT7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CNOT7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT7 BINDING SITE1 and CNOT7 BINDING SITE2, designated SEQ ID:15001 and SEQ ID:13526 respectively, to the nu-

cleotide sequence of VGAM1944 RNA, herein designated VGAM RNA, also designated SEQ ID:4655.

[65631] Another function of VGAM1944 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 7 (CNOT7, Accession NM\_013354). Accordingly, utilities of VGAM1944 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT7. FLJ13769 (Accession NM\_025012) is another VGAM1944 host target gene. FLJ13769 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13769, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13769 BINDING SITE, designated SEQ ID:24597, to the nucleotide sequence of VGAM1944 RNA, herein designated VGAM RNA, also designated SEQ ID:4655.

[65632] Another function of VGAM1944 is therefore inhibition of FLJ13769 (Accession NM\_025012). Accordingly, utilities of VGAM1944 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13769. KIAA0750 (Accession NM\_014632) is another VGAM1944 host target gene. KIAA0750 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0750 BINDING SITE, designated SEQ ID:16000, to the nucleotide sequence of VGAM1944 RNA, herein designated VGAM RNA, also designated SEQ ID:4655.

[65633] Another function of VGAM1944 is therefore inhibition of KIAA0750 (Accession NM\_014632). Accordingly, utilities of VGAM1944 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0750. Sp2 Transcription Factor (SP2, Accession NM\_003110) is another VGAM1944 host target gene. SP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP2 BINDING SITE, designated SEQ ID:9079, to the nucleotide sequence of VGAM1944 RNA, herein designated VGAM RNA, also designated SEQ ID:4655.

[65634] Another function of VGAM1944 is therefore inhibition of

Sp2 Transcription Factor (SP2, Accession NM\_003110). Accordingly, utilities of VGAM1944 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP2. LOC120772 (Accession XM\_058505) is another VGAM1944 host target gene. LOC120772 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC120772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120772 BINDING SITE, designated SEQ ID:36627, to the nucleotide sequence of VGAM1944 RNA, herein designated VGAM RNA, also designated SEQ ID:4655.

[65635] Another function of VGAM1944 is therefore inhibition of LOC120772 (Accession XM\_058505). Accordingly, utilities of VGAM1944 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120772. LOC147929 (Accession XM\_085961) is another VGAM1944 host target gene. LOC147929 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC147929, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147929 BINDING SITE, designated SEQ ID:38419, to the nucleotide sequence of VGAM1944 RNA, herein designated VGAM RNA, also designated SEQ ID:4655.

[65636] Another function of VGAM1944 is therefore inhibition of LOC147929 (Accession XM\_085961). Accordingly, utilities of VGAM1944 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147929. LOC256867 (Accession XM\_170694) is another VGAM1944 host target gene. LOC256867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256867 BINDING SITE, designated SEQ ID:45470, to the nucleotide sequence of VGAM1944 RNA, herein designated VGAM RNA, also designated SEQ ID:4655.

[65637] Another function of VGAM1944 is therefore inhibition of LOC256867 (Accession XM\_170694). Accordingly, utilities of VGAM1944 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC256867. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1945 (VGAM1945) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65638] VGAM1945 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1945 was detected is described hereinabove with reference to Figs. 1–8.

[65639] VGAM1945 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1945 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65640] VGAM1945 gene encodes a VGAM1945 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1945 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1945 precursor RNA is designated SEQ ID:1931, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1931 is located at position 7746 relative to the genome of Variola Virus.

- [65641] VGAM1945 precursor RNA folds onto itself, forming VGAM1945 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [65642] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1945 folded precursor RNA into VGAM1945 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1945 RNA is designated SEQ ID:4656, and is provided hereinbelow with reference to the sequence listing part.

[65643] VGAM1945 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1945 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1945 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65644] VGAM1945 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1945 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1945 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1945 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1945 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65645] The complementary binding of VGAM1945 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1945 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1945 host target RNA into VGAM1945 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65646] It is appreciated that VGAM1945 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1945 host target genes. The mRNA of each one of this plurality of VGAM1945 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1945 RNA, herein designated VGAM RNA, and which when bound by VGAM1945 RNA causes

inhibition of translation of respective one or more VGAM1945 host target proteins.

[65647] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1945 gene, herein designated VGAM GENE, on one or more VGAM1945 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65648] It is yet further appreciated that a function of VGAM1945 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1945 include diagnosis, prevention and

treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1945 correlate with, and may be deduced from, the identity of the host target genes which VGAM1945 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65649] Nucleotide sequences of the VGAM1945 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1945 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1945 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1945 are further described hereinbelow with reference to Table 1.

[65650] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1945 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1945 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65651] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1945 gene, herein designated VGAM is inhibition of expression of VGAM1945 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1945 correlate with, and may be deduced from, the identity of the target genes which VGAM1945 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65652] Retinitis Pigmentosa 2 (X-linked recessive) (RP2, Accession NM\_006915) is a VGAM1945 host target gene. RP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP2 BINDING SITE, designated SEQ ID:13790, to the nucleotide sequence of VGAM1945 RNA, herein designated VGAM RNA, also designated SEQ ID:4656.

[65653] A function of VGAM1945 is therefore inhibition of Retinitis Pigmentosa 2 (X-linked recessive) (RP2, Accession NM\_006915). Accordingly, utilities of VGAM1945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP2. caspr5 (Accession NM\_130773) is another VGAM1945 host target gene. caspr5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

caspr5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of caspr5 BINDING SITE, designated SEQ ID:28267, to the nucleotide sequence of VGAM1945 RNA, herein designated VGAM RNA, also designated SEQ ID:4656.

[65654] Another function of VGAM1945 is therefore inhibition of caspr5 (Accession NM\_130773). Accordingly, utilities of VGAM1945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with caspr5. FLJ11252 (Accession XM\_041702) is another VGAM1945 host target gene. FLJ11252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11252 BINDING SITE, designated SEQ ID:33566, to the nucleotide sequence of VGAM1945 RNA, herein designated VGAM RNA, also designated SEQ ID:4656.

[65655] Another function of VGAM1945 is therefore inhibition of FLJ11252 (Accession XM\_041702). Accordingly, utilities of



VGAM1945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11252. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1946 (VGAM1946) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65656] VGAM1946 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1946 was detected is described hereinabove with reference to Figs. 1–8.

[65657] VGAM1946 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus.

VGAM1946 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65658] VGAM1946 gene encodes a VGAM1946 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1946 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu–

cleotide sequence of VGAM1946 precursor RNA is designated SEQ ID:1932, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1932 is located at position 11538 relative to the genome of Variola Virus.

[65659] VGAM1946 precursor RNA folds onto itself, forming VGAM1946 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65660] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1946 folded precursor RNA into VGAM1946 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1946 RNA is designated SEQ ID:4657, and

is provided hereinbelow with reference to the sequence listing part.

[65661] VGAM1946 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1946 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1946 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65662] VGAM1946 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1946 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1946 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1946 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1946 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65663] The complementary binding of VGAM1946 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1946 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1946 host target RNA into VGAM1946 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65664] It is appreciated that VGAM1946 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1946 host target genes. The mRNA of each one of this plurality of VGAM1946 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1946 RNA, herein designated VGAM RNA, and which when bound by VGAM1946 RNA causes inhibition of translation of respective one or more VGAM1946 host target proteins.

[65665] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1946 gene, herein designated VGAM GENE, on one or more VGAM1946 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65666] It is yet further appreciated that a function of VGAM1946 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1946 correlate with, and may be deduced from, the identity of the host target genes which VGAM1946 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65667] Nucleotide sequences of the VGAM1946 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1946 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1946 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1946 are further described hereinbelow with reference to Table 1.

[65668] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1946 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1946 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65669] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1946 gene, herein designated VGAM is inhibition of expression of VGAM1946 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1946 correlate with, and may be deduced from, the identity of the target genes which VGAM1946 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65670] Angiotensin II Receptor, Type 1 (AGTR1, Accession NM\_000685) is a VGAM1946 host target gene. AGTR1 BINDING SITE1 through AGTR1 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AGTR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGTR1 BINDING SITE1 through AGTR1 BINDING SITE5, designated SEQ ID:6343, SEQ ID:11244, SEQ ID:14310, SEQ ID:25595 and SEQ ID:25770 respectively, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65671] A function of VGAM1946 is therefore inhibition of Angiotensin II Receptor, Type 1 (AGTR1, Accession NM\_000685), a gene which is an important effector con-

trolling blood pressure and volume in the cardiovascular system. Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGTR1. The function of AGTR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM96.Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542) is another VGAM1946 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45231, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65672] Another function of VGAM1946 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM\_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utili-



ties of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. MAP-kinase Activating Death Domain (MADD, Accession NM\_130471) is another VGAM1946 host target gene. MADD BINDING SITE1 through MADD BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MADD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADD BINDING SITE1 through MADD BINDING SITE6, designated SEQ ID:28241, SEQ ID:28246, SEQ ID:28251, SEQ ID:28256, SEQ ID:9786 and SEQ ID:28235 respectively, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65673] Another function of VGAM1946 is therefore inhibition of MAP-kinase Activating Death Domain (MADD, Accession NM\_130471), a gene which may regulate two different pathways for neural activities. interacts with the type-1 tu-

mor necrosis factor receptor (TNFR1); death domain-containing protein. Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADD. The function of MADD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430. Ribulose-5-phosphate-3-epimerase (RPE, Accession XM\_030834) is another VGAM1946 host target gene. RPE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPE BINDING SITE, designated SEQ ID:31158, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65674] Another function of VGAM1946 is therefore inhibition of Ribulose-5-phosphate-3-epimerase (RPE, Accession XM\_030834). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPE. Solute Carrier Family 6 (neurotransmitter transporter, dopamine), Member 3

(SLC6A3, Accession NM\_001044) is another VGAM1946 host target gene. SLC6A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A3 BINDING SITE, designated SEQ ID:6712, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65675] Another function of VGAM1946 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, dopamine), Member 3 (SLC6A3, Accession NM\_001044), a gene which terminates the action of dopamine by its high affinity sodium-dependent reuptake into presynaptic terminals. Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A3. The function of SLC6A3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1753. Tec Protein Tyrosine Kinase (TEC, Accession NM\_003215) is another VGAM1946 host target gene. TEC

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEC BINDING SITE, designated SEQ ID:9220, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65676] Another function of VGAM1946 is therefore inhibition of Tec Protein Tyrosine Kinase (TEC, Accession NM\_003215). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEC. Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM\_021083) is another VGAM1946 host target gene. XK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XK BINDING SITE, designated SEQ ID:22053, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65677] Another function of VGAM1946 is therefore inhibition of Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM\_021083). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XK. Cyldromatosis (turban tumor syndrome) (CYLD, Accession NM\_015247) is another VGAM1946 host target gene. CYLD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYLD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYLD BINDING SITE, designated SEQ ID:17576, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65678] Another function of VGAM1946 is therefore inhibition of Cyldromatosis (turban tumor syndrome) (CYLD, Accession NM\_015247). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYLD. FLJ10925 (Accession NM\_018275) is another VGAM1946 host target gene. FLJ10925 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by FLJ10925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10925 BINDING SITE, designated SEQ ID:20261, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65679] Another function of VGAM1946 is therefore inhibition of FLJ10925 (Accession NM\_018275). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10925. FLJ11274 (Accession NM\_018375) is another VGAM1946 host target gene. FLJ11274 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11274 BINDING SITE, designated SEQ ID:20400, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65680] Another function of VGAM1946 is therefore inhibition of FLJ11274 (Accession NM\_018375). Accordingly, utilities of

VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11274. KIAA0161 (Accession NM\_014746) is another VGAM1946 host target gene. KIAA0161 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0161 BINDING SITE, designated SEQ ID:16435, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65681] Another function of VGAM1946 is therefore inhibition of KIAA0161 (Accession NM\_014746). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0161. MGC15438 (Accession NM\_032874) is another VGAM1946 host target gene. MGC15438 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC15438 BINDING SITE, designated SEQ ID:26694, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65682] Another function of VGAM1946 is therefore inhibition of MGC15438 (Accession NM\_032874). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15438. PRO2214 (Accession NM\_018517) is another VGAM1946 host target gene. PRO2214 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO2214, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2214 BINDING SITE, designated SEQ ID:20588, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65683] Another function of VGAM1946 is therefore inhibition of PRO2214 (Accession NM\_018517). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2214. Solute Carrier Family 21 (organic anion transporter), Member 14 (SLC21A14, Accession NM\_017435) is



another VGAM1946 host target gene. SLC21A14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC21A14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC21A14 BINDING SITE, designated SEQ ID:18892, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65684] Another function of VGAM1946 is therefore inhibition of Solute Carrier Family 21 (organic anion transporter), Member 14 (SLC21A14, Accession NM\_017435). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC21A14. X123 (Accession XM\_046023) is another VGAM1946 host target gene. X123 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by X123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of X123 BINDING SITE, designated SEQ ID:34651, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA,

also designated SEQ ID:4657.

[65685] Another function of VGAM1946 is therefore inhibition of X123 (Accession XM\_046023). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with X123. LOC120856 (Accession XM\_058509) is another VGAM1946 host target gene. LOC120856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120856 BINDING SITE, designated SEQ ID:36646, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65686] Another function of VGAM1946 is therefore inhibition of LOC120856 (Accession XM\_058509). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120856. LOC153339 (Accession XM\_098362) is another VGAM1946 host target gene. LOC153339 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153339, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153339 BINDING SITE, designated SEQ ID:41616, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65687] Another function of VGAM1946 is therefore inhibition of LOC153339 (Accession XM\_098362). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153339. LOC159091 (Accession NM\_138819) is another VGAM1946 host target gene. LOC159091 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC159091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159091 BINDING SITE, designated SEQ ID:29038, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65688] Another function of VGAM1946 is therefore inhibition of LOC159091 (Accession NM\_138819). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC159091. LOC255520 (Accession XM\_171073) is another VGAM1946 host target gene. LOC255520 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255520 BINDING SITE, designated SEQ ID:45881, to the nucleotide sequence of VGAM1946 RNA, herein designated VGAM RNA, also designated SEQ ID:4657.

[65689] Another function of VGAM1946 is therefore inhibition of LOC255520 (Accession XM\_171073). Accordingly, utilities of VGAM1946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255520. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1947 (VGAM1947) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65690] VGAM1947 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1947 was detected is described hereinabove with reference to Figs. 1–8.

[65691] VGAM1947 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus.

VGAM1947 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65692] VGAM1947 gene encodes a VGAM1947 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1947 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1947 precursor RNA is designated SEQ ID:1933, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1933 is located at position 16704 relative to the genome of Variola Virus.

[65693] VGAM1947 precursor RNA folds onto itself, forming VGAM1947 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65694] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1947 folded precursor RNA into VGAM1947 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 68%) nucleotide sequence of VGAM1947 RNA is designated SEQ ID:4658, and is provided hereinbelow with reference to the sequence listing part.

[65695] VGAM1947 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1947 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1947 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65696] VGAM1947 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1947 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1947 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1947 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1947 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65697] The complementary binding of VGAM1947 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1947 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1947 host target RNA into VGAM1947 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65698] It is appreciated that VGAM1947 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1947 host target genes. The mRNA of each one of this plurality of VGAM1947 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1947 RNA, herein designated VGAM RNA, and which when bound by VGAM1947 RNA causes inhibition of translation of respective one or more VGAM1947 host target proteins.

[65699] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1947 gene, herein designated VGAM GENE, on one or more VGAM1947 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65700] It is yet further appreciated that a function of VGAM1947 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1947 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1947 correlate with, and may be deduced from, the identity of the host target genes which VGAM1947 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65701] Nucleotide sequences of the VGAM1947 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1947 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1947 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1947 are further described hereinbelow with reference to Table 1.

[65702] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1947 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1947 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65703] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1947 gene, herein designated VGAM is inhibition of expression of VGAM1947 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1947 correlate with, and may be deduced from, the identity of the target genes which VGAM1947 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65704] Solute Carrier Family 19 (thiamine transporter), Member 2 (SLC19A2, Accession XM\_044421) is a VGAM1947 host target gene. SLC19A2 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by SLC19A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC19A2 BINDING SITE, designated SEQ ID:34194, to the nucleotide sequence of VGAM1947 RNA, herein designated VGAM RNA, also designated SEQ ID:4658.

[65705] A function of VGAM1947 is therefore inhibition of Solute Carrier Family 19 (thiamine transporter), Member 2 (SLC19A2, Accession XM\_044421). Accordingly, utilities of VGAM1947 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC19A2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1948 (VGAM1948) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65706] VGAM1948 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1948 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[65707] VGAM1948 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Paramyxovirus 6. VGAM1948 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65708] VGAM1948 gene encodes a VGAM1948 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1948 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1948 precursor RNA is designated SEQ ID:1934, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1934 is located at position 4256 relative to the genome of Avian Paramyxovirus 6.

[65709] VGAM1948 precursor RNA folds onto itself, forming VGAM1948 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65710] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1948 folded precursor RNA into VGAM1948 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1948 RNA is designated SEQ ID:4659, and is provided hereinbelow with reference to the sequence listing part.

[65711] VGAM1948 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1948 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1948 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65712] VGAM1948 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1948 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1948 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1948 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1948 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65713] The complementary binding of VGAM1948 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1948 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1948 host target RNA into VGAM1948 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65714] It is appreciated that VGAM1948 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1948 host target genes. The mRNA of each one of this plurality of VGAM1948 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1948 RNA, herein designated VGAM RNA, and which when bound by VGAM1948 RNA causes inhibition of translation of respective one or more VGAM1948 host target proteins.

[65715] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1948 gene, herein designated VGAM GENE, on one or more VGAM1948 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65716] It is yet further appreciated that a function of VGAM1948 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1948 include diagnosis, prevention and treatment of viral infection by Avian Paramyxovirus 6. Specific functions, and accordingly utilities, of VGAM1948 correlate with, and may be deduced from, the identity of the host target genes which VGAM1948 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65717] Nucleotide sequences of the VGAM1948 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1948 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding



of VGAM1948 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1948 are further described hereinbelow with reference to Table 1.

[65718] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1948 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1948 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65719] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1948 gene, herein designated VGAM is inhibition of expression of VGAM1948 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1948 correlate with, and may be deduced from, the identity of the target genes which VGAM1948 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65720] ATP-binding Cassette, Sub-family G (WHITE), Member 1 (ABCG1, Accession NM\_004915) is a VGAM1948 host target gene. ABCG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCG1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCG1 BINDING SITE, designated SEQ ID:11351, to the nucleotide sequence of VGAM1948 RNA, herein designated VGAM RNA, also designated SEQ ID:4659.

[65721] A function of VGAM1948 is therefore inhibition of ATP-binding Cassette, Sub-family G (WHITE), Member 1 (ABCG1, Accession NM\_004915), a gene which transporter involved in macrophage lipid homeostasis. Accordingly, utilities of VGAM1948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCG1. The function of ABCG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM595.C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252) is another VGAM1948 host target gene. CLECSF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLECSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of CLECSF5 BINDING SITE, designated SEQ ID:14917, to the nucleotide sequence of VGAM1948 RNA, herein designated VGAM RNA, also designated SEQ ID:4659.

[65722] Another function of VGAM1948 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252). Accordingly, utilities of VGAM1948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF5.

2'-5'-oligoadenylate Synthetase 3, 100kDa (OAS3, Accession NM\_006187) is another VGAM1948 host target gene. OAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAS3 BINDING SITE, designated SEQ ID:12858, to the nucleotide sequence of VGAM1948 RNA, herein designated VGAM RNA, also designated SEQ ID:4659.

[65723] Another function of VGAM1948 is therefore inhibition of 2'-5'-oligoadenylate Synthetase 3, 100kDa (OAS3, Accession NM\_006187), a gene which may play a role in medi-

ating resistance to virus infection, control of cell growth, differentiation, and apoptosis. Accordingly, utilities of VGAM1948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAS3. The function of OAS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM309. Polymerase (DNA directed), Eta (POLH, Accession NM\_006502) is another VGAM1948 host target gene. POLH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POLH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLH BINDING SITE, designated SEQ ID:13249, to the nucleotide sequence of VGAM1948 RNA, herein designated VGAM RNA, also designated SEQ ID:4659.

[65724] Another function of VGAM1948 is therefore inhibition of Polymerase (DNA directed), Eta (POLH, Accession NM\_006502). Accordingly, utilities of VGAM1948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLH. HSA249128 (Accession NM\_017583) is another VGAM1948 host target

gene. HSA249128 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HSA249128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA249128 BINDING SITE, designated SEQ ID:19024, to the nucleotide sequence of VGAM1948 RNA, herein designated VGAM RNA, also designated SEQ ID:4659.

[65725] Another function of VGAM1948 is therefore inhibition of HSA249128 (Accession NM\_017583). Accordingly, utilities of VGAM1948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA249128. MGC4655 (Accession NM\_033309) is another VGAM1948 host target gene. MGC4655 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC4655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4655 BINDING SITE, designated SEQ ID:27145, to the nucleotide sequence of VGAM1948 RNA, herein designated VGAM RNA, also designated SEQ ID:4659.

[65726] Another function of VGAM1948 is therefore inhibition of MGC4655 (Accession NM\_033309). Accordingly, utilities of VGAM1948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4655. Transducer of ERBB2, 2 (TOB2, Accession XM\_170995) is another VGAM1948 host target gene. TOB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOB2 BINDING SITE, designated SEQ ID:45763, to the nucleotide sequence of VGAM1948 RNA, herein designated VGAM RNA, also designated SEQ ID:4659.

[65727] Another function of VGAM1948 is therefore inhibition of Transducer of ERBB2, 2 (TOB2, Accession XM\_170995). Accordingly, utilities of VGAM1948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOB2. LOC90917 (Accession XM\_034861) is another VGAM1948 host target gene. LOC90917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90917, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90917 BINDING SITE, designated SEQ ID:32168, to the nucleotide sequence of VGAM1948 RNA, herein designated VGAM RNA, also designated SEQ ID:4659.

[65728] Another function of VGAM1948 is therefore inhibition of LOC90917 (Accession XM\_034861). Accordingly, utilities of VGAM1948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90917. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1949 (VGAM1949) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65729] VGAM1949 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1949 was detected is described hereinabove with reference to Figs. 1-8.

[65730] VGAM1949 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Paramyxovirus 6.

VGAM1949 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65731] VGAM1949 gene encodes a VGAM1949 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1949 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1949 precursor RNA is designated SEQ ID:1935, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1935 is located at position 14249 relative to the genome of Avian Paramyxovirus 6.

[65732] VGAM1949 precursor RNA folds onto itself, forming VGAM1949 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65733] An enzyme complex designated DICER COMPLEX, `dices`



the VGAM1949 folded precursor RNA into VGAM1949 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1949 RNA is designated SEQ ID:4660, and is provided hereinbelow with reference to the sequence listing part.

[65734] VGAM1949 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1949 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1949 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65735] VGAM1949 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1949 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1949 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1949 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1949 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65736] The complementary binding of VGAM1949 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1949 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1949 host target RNA into VGAM1949 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65737] It is appreciated that VGAM1949 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1949 host target genes. The mRNA of each one of this plurality of VGAM1949 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1949 RNA, herein designated VGAM RNA, and which when bound by VGAM1949 RNA causes inhibition of translation of respective one or more VGAM1949 host target proteins.

[65738] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1949 gene, herein designated VGAM GENE, on one or more VGAM1949 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65739] It is yet further appreciated that a function of VGAM1949 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1949 include diagnosis, prevention and treatment of viral infection by Avian Paramyxovirus 6. Specific functions, and accordingly utilities, of VGAM1949 correlate with, and may be deduced from, the identity of the host target genes which VGAM1949 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65740] Nucleotide sequences of the VGAM1949 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1949 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1949 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1949 are further described hereinbelow with reference to Table 1.

[65741] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1949 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1949 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65742] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1949 gene, herein designated VGAM is inhibition of expression of VGAM1949 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1949 correlate with, and may be deduced from, the identity of the target genes which VGAM1949 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65743] Keratocan (KERA, Accession NM\_007035) is a VGAM1949 host target gene. KERA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KERA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KERA BINDING SITE, designated SEQ ID:13905, to the nucleotide sequence of VGAM1949

RNA, herein designated VGAM RNA, also designated SEQ ID:4660.

[65744] A function of VGAM1949 is therefore inhibition of Keratocan (KERA, Accession NM\_007035), a gene which may be important in developing and maintaining corneal transparency and for the structure of the stromal matrix. Accordingly, utilities of VGAM1949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KERA. The function of KERA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM723. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1950 (VGAM1950) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65745] VGAM1950 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1950 was detected is described hereinabove with reference to Figs. 1-8.

[65746] VGAM1950 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Avian Paramyxovirus 6. VGAM1950 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65747] VGAM1950 gene encodes a VGAM1950 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1950 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1950 precursor RNA is designated SEQ ID:1936, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1936 is located at position 14024 relative to the genome of Avian Paramyxovirus 6.

[65748] VGAM1950 precursor RNA folds onto itself, forming VGAM1950 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65749] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1950 folded precursor RNA into VGAM1950 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1950 RNA is designated SEQ ID:4661, and is provided hereinbelow with reference to the sequence listing part.

[65750] VGAM1950 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1950 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1950 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65751] VGAM1950 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1950 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM1950 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1950 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1950 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65752] The complementary binding of VGAM1950 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1950 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1950

host target RNA into VGAM1950 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65753] It is appreciated that VGAM1950 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1950 host target genes. The mRNA of each one of this plurality of VGAM1950 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1950 RNA, herein designated VGAM RNA, and which when bound by VGAM1950 RNA causes inhibition of translation of respective one or more VGAM1950 host target proteins.

[65754] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1950 gene, herein designated VGAM GENE, on one or more VGAM1950 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65755] It is yet further appreciated that a function of VGAM1950 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of viral infection by Avian Paramyxovirus 6. Specific functions, and accordingly utilities, of VGAM1950 correlate with, and may be deduced from, the identity of the host target genes which VGAM1950 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65756] Nucleotide sequences of the VGAM1950 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1950 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1950 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1950 are further

described hereinbelow with reference to Table 1.

[65757] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1950 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1950 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65758] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1950 gene, herein designated VGAM is inhibition of expression of VGAM1950 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1950 correlate with, and may be deduced from, the identity of the target genes which VGAM1950 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65759] Cytochrome P450, Subfamily IVF, Polypeptide 3 (leukotriene B4 omega hydroxylase) (CYP4F3, Accession NM\_000896) is a VGAM1950 host target gene. CYP4F3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP4F3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of CYP4F3 BINDING SITE, designated SEQ ID:6594, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65760] A function of VGAM1950 is therefore inhibition of Cytochrome P450, Subfamily IVF, Polypeptide 3 (leukotriene B4 omega hydroxylase) (CYP4F3, Accession NM\_000896), a gene which converts leukotriene B4 into the less active 20-hydroxy-leukotriene B4. Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP4F3. The function of CYP4F3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM186. Coagulation Factor II (thrombin) Receptor-like 3 (F2RL3, Accession NM\_003950) is another VGAM1950 host target gene. F2RL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by F2RL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F2RL3 BINDING SITE, designated SEQ ID:10085, to the nucleotide sequence of

VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65761] Another function of VGAM1950 is therefore inhibition of Coagulation Factor II (thrombin) Receptor-like 3 (F2RL3, Accession NM\_003950), a gene which Protease-activated receptor 4; G protein-coupled receptor that increases phosphoinositide hydrolysis. Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F2RL3. The function of F2RL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM193. Mature T-cell Proliferation 1 (MTCP1, Accession NM\_014221) is another VGAM1950 host target gene. MTCP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MTCP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTCP1 BINDING SITE, designated SEQ ID:15488, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65762] Another function of VGAM1950 is therefore inhibition of Mature T-cell Proliferation 1 (MTCP1, Accession NM\_014221). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTCP1. Adaptor-related Protein Complex 4, Sigma 1 Subunit (AP4S1, Accession NM\_007077) is another VGAM1950 host target gene. AP4S1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP4S1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP4S1 BINDING SITE, designated SEQ ID:13941, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65763] Another function of VGAM1950 is therefore inhibition of Adaptor-related Protein Complex 4, Sigma 1 Subunit (AP4S1, Accession NM\_007077). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP4S1. Caspase Recruitment Domain Family, Member 14 (CARD14, Accession NM\_024110) is another VGAM1950

host target gene. CARD14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARD14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARD14 BINDING SITE, designated SEQ ID:23556, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65764] Another function of VGAM1950 is therefore inhibition of Caspase Recruitment Domain Family, Member 14 (CARD14, Accession NM\_024110). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARD14. KIAA0844 (Accession NM\_014951) is another VGAM1950 host target gene. KIAA0844 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0844, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0844 BINDING SITE, designated SEQ ID:17287, to the nucleotide sequence of VGAM1950 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4661.

[65765] Another function of VGAM1950 is therefore inhibition of KIAA0844 (Accession NM\_014951). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0844. KIAA1952 (Accession XM\_054983) is another VGAM1950 host target gene. KIAA1952 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1952, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1952 BINDING SITE, designated SEQ ID:36220, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65766] Another function of VGAM1950 is therefore inhibition of KIAA1952 (Accession XM\_054983). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1952. Lipase, Endothelial (LIPG, Accession NM\_006033) is another VGAM1950 host target gene. LIPG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIPG, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIPG BINDING SITE, designated SEQ ID:12655, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65767] Another function of VGAM1950 is therefore inhibition of Lipase, Endothelial (LIPG, Accession NM\_006033). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIPG. Mitochondrial Ribosomal Protein S10 (MRPS10, Accession NM\_018141) is another VGAM1950 host target gene. MRPS10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPS10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS10 BINDING SITE, designated SEQ ID:19940, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65768] Another function of VGAM1950 is therefore inhibition of Mitochondrial Ribosomal Protein S10 (MRPS10, Accession

NM\_018141). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS10. Zinc Finger Protein 297B (ZNF297B, Accession NM\_014007) is another VGAM1950 host target gene. ZNF297B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF297B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF297B BINDING SITE, designated SEQ ID:15222, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65769] Another function of VGAM1950 is therefore inhibition of Zinc Finger Protein 297B (ZNF297B, Accession NM\_014007). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF297B. LOC113523 (Accession XM\_054378) is another VGAM1950 host target gene. LOC113523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC113523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113523 BINDING SITE, designated SEQ ID:36153, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65770] Another function of VGAM1950 is therefore inhibition of LOC113523 (Accession XM\_054378). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113523. LOC145387 (Accession XM\_096791) is another VGAM1950 host target gene. LOC145387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145387 BINDING SITE, designated SEQ ID:40539, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65771] Another function of VGAM1950 is therefore inhibition of LOC145387 (Accession XM\_096791). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC145387. LOC153577 (Accession XM\_098394) is another VGAM1950 host target gene. LOC153577 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153577 BINDING SITE, designated SEQ ID:41645, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65772] Another function of VGAM1950 is therefore inhibition of LOC153577 (Accession XM\_098394). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153577. LOC199733 (Accession XM\_117123) is another VGAM1950 host target gene. LOC199733 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199733, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199733 BINDING SITE, designated SEQ ID:43246, to the nucleotide sequence of VGAM1950 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4661.

[65773] Another function of VGAM1950 is therefore inhibition of LOC199733 (Accession XM\_117123). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199733. LOC221822 (Accession XM\_167268) is another VGAM1950 host target gene. LOC221822 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221822, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221822 BINDING SITE, designated SEQ ID:44624, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65774] Another function of VGAM1950 is therefore inhibition of LOC221822 (Accession XM\_167268). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221822. LOC92973 (Accession XM\_048529) is another VGAM1950 host target gene. LOC92973 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92973, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92973 BINDING SITE, designated SEQ ID:35187, to the nucleotide sequence of VGAM1950 RNA, herein designated VGAM RNA, also designated SEQ ID:4661.

[65775] Another function of VGAM1950 is therefore inhibition of LOC92973 (Accession XM\_048529). Accordingly, utilities of VGAM1950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92973. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1951 (VGAM1951) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65776] VGAM1951 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1951 was detected is described hereinabove with reference to Figs. 1-8.

[65777] VGAM1951 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Paramyxovirus 6.

VGAM1951 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65778] VGAM1951 gene encodes a VGAM1951 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1951 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1951 precursor RNA is designated SEQ ID:1937, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1937 is located at position 5552 relative to the genome of Avian Paramyxovirus 6.

[65779] VGAM1951 precursor RNA folds onto itself, forming VGAM1951 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65780] An enzyme complex designated DICER COMPLEX, `dices`



the VGAM1951 folded precursor RNA into VGAM1951 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1951 RNA is designated SEQ ID:4662, and is provided hereinbelow with reference to the sequence listing part.

[65781] VGAM1951 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1951 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1951 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65782] VGAM1951 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1951 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1951 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1951 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1951 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65783] The complementary binding of VGAM1951 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1951 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1951 host target RNA into VGAM1951 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65784] It is appreciated that VGAM1951 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1951 host target genes. The mRNA of each one of this plurality of VGAM1951 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1951 RNA, herein designated VGAM RNA, and which when bound by VGAM1951 RNA causes inhibition of translation of respective one or more VGAM1951 host target proteins.

[65785] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1951 gene, herein designated VGAM GENE, on one or more VGAM1951 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65786] It is yet further appreciated that a function of VGAM1951 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1951 include diagnosis, prevention and treatment of viral infection by Avian Paramyxovirus 6. Specific functions, and accordingly utilities, of VGAM1951 correlate with, and may be deduced from, the identity of the host target genes which VGAM1951 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65787] Nucleotide sequences of the VGAM1951 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1951 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1951 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1951 are further described hereinbelow with reference to Table 1.

[65788] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1951 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1951 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65789] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1951 gene, herein designated VGAM is inhibition of expression of VGAM1951 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1951 correlate with, and may be deduced from, the identity of the target genes which VGAM1951 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65790] ATP-binding Cassette, Sub-family B (MDR/TAP), Member 9 (ABCB9, Accession NM\_019625) is a VGAM1951 host target gene. ABCB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCB9 BINDING SITE, designated SEQ

ID:21241, to the nucleotide sequence of VGAM1951 RNA, herein designated VGAM RNA, also designated SEQ ID:4662.

[65791] A function of VGAM1951 is therefore inhibition of ATP-binding Cassette, Sub-family B (MDR/TAP), Member 9 (ABCB9, Accession NM\_019625), a gene which ATP binding cassette transporter B9; has transmembrane domain, nucleotide-binding domain with Walker motifs. Accordingly, utilities of VGAM1951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCB9. The function of ABCB9 has been established by previous studies. For background information on the ATP-binding cassette (ABC) family of transporter proteins, see ABCA4 (OMIM Ref. No. 601691). In addition to the 'full' ABC transporters with 2 transmembrane domains and 2 nucleotide-binding domains, there are 'half' proteins that contain only 1 of each domain (e.g., ABCB1; 171050). Full transporters are usually found in the plasma membrane, whereas half transporters are found in subcellular organelles. By searching an EST database and screening a T-lymphoblast cDNA library, Zhang et al. (2000) obtained a cDNA encoding ABCB9. Sequence analysis predicted that the 766-amino acid ABCB9 protein has

10 potential N-terminal transmembrane segments. ABCB9 shares 94% identity with the rodent sequences and is approximately 39% identical to 2 human endoplasmic reticulum half transporters, TAP1 (ABCB2; 170260) and TAP2 (ABCB3; 170261). RT-PCR and genomic sequence analysis established the existence of a splice variant with a 129-bp deletion expressed in testis and brain. Northern blot analysis detected low expression of a 3.7-kb transcript in most tissues tested, with an additional 2.2-kb transcript detected in tissues with relatively high expression, such as testis. Western blot analysis showed expression of a 72-kD nonglycosylated protein, significantly smaller than the predicted mass of 84.5 kD, that was enriched in lysosomes. Immunofluorescence microscopy demonstrated colocalization of ABCB9 with the lysosomal proteins LAMP1 (OMIM Ref. No. 153330) and LAMP2 (OMIM Ref. No. 309060). Immunohistochemical analysis detected ABCB9 expression in Sertoli cells of rodent seminiferous tubules. Allikmets et al. (1996) mapped an EST corresponding to the ABCB9 gene to 12q24.

[65792] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [65793] Allikmets, R.; Gerrard, B.; Hutchinson, A.; Dean, M. : Characterization of the human ABC superfamily: isolation and mapping of 21 new genes using the expressed sequence tags database. Hum. Molec. Genet. 5: 1649–1655, 1996. ; and
- [65794] Zhang, F.; Zhang, W.; Liu, L.; Fisher, C. L.; Hui, D.; Childs, S.; Dorovini-Zis, K.; Ling, V. : Characterization of ABCB9, an ATP binding cassette protein associated with lysosomes. J.
- [65795] Further studies establishing the function and utilities of ABCB9 are found in John Hopkins OMIM database record ID 605453, and in cited publications numbered 2822 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. A Disintegrin and Metalloproteinase Domain 17 (tumor necrosis factor, alpha, converting enzyme) (ADAM17, Accession NM\_021832) is another VGAM1951 host target gene. ADAM17 BINDING SITE1 and ADAM17 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADAM17, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM17 BIND-



ING SITE1 and ADAM17 BINDING SITE2, designated SEQ ID:22408 and SEQ ID:9155 respectively, to the nucleotide sequence of VGAM1951 RNA, herein designated VGAM RNA, also designated SEQ ID:4662.

[65796] Another function of VGAM1951 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 17 (tumor necrosis factor, alpha, converting enzyme) (ADAM17, Accession NM\_021832), a gene which member of ADAM family of zinc metalloproteases. Accordingly, utilities of VGAM1951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM17. The function of ADAM17 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM264. Fucosyltransferase 9 (alpha (1,3) Fucosyltransferase) (FUT9, Accession XM\_042167) is another VGAM1951 host target gene. FUT9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT9 BINDING SITE, designated SEQ ID:33698, to the nucleotide se-

quence of VGAM1951 RNA, herein designated VGAM RNA, also designated SEQ ID:4662.

[65797] Another function of VGAM1951 is therefore inhibition of Fucosyltransferase 9 (alpha (1,3) Fucosyltransferase) (FUT9, Accession XM\_042167), a gene which catalyzes alpha-1,3 glycosidic linkages. Accordingly, utilities of VGAM1951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT9. The function of FUT9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Chromosome 20 Open Reading Frame 126 (C20orf126, Accession NM\_030815) is another VGAM1951 host target gene. C20orf126 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf126, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf126 BINDING SITE, designated SEQ ID:25135, to the nucleotide sequence of VGAM1951 RNA, herein designated VGAM RNA, also designated SEQ ID:4662.

[65798] Another function of VGAM1951 is therefore inhibition of

Chromosome 20 Open Reading Frame 126 (C20orf126, Accession NM\_030815). Accordingly, utilities of VGAM1951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf126. Chloride Intracellular Channel 5 (CLIC5, Accession NM\_016929) is another VGAM1951 host target gene. CLIC5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLIC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIC5 BINDING SITE, designated SEQ ID:18846, to the nucleotide sequence of VGAM1951 RNA, herein designated VGAM RNA, also designated SEQ ID:4662.

[65799] Another function of VGAM1951 is therefore inhibition of Chloride Intracellular Channel 5 (CLIC5, Accession NM\_016929). Accordingly, utilities of VGAM1951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIC5. FLJ31890 (Accession XM\_166117) is another VGAM1951 host target gene. FLJ31890 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31890, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31890 BINDING SITE, designated SEQ ID:43894, to the nucleotide sequence of VGAM1951 RNA, herein designated VGAM RNA, also designated SEQ ID:4662.

[65800] Another function of VGAM1951 is therefore inhibition of FLJ31890 (Accession XM\_166117). Accordingly, utilities of VGAM1951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31890. KIAA0365 (Accession XM\_086055) is another VGAM1951 host target gene. KIAA0365 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0365, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0365 BINDING SITE, designated SEQ ID:38470, to the nucleotide sequence of VGAM1951 RNA, herein designated VGAM RNA, also designated SEQ ID:4662.

[65801] Another function of VGAM1951 is therefore inhibition of KIAA0365 (Accession XM\_086055). Accordingly, utilities of VGAM1951 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0365. PR Domain Containing 13 (PRDM13, Accession NM\_021620) is another VGAM1951 host target gene. PRDM13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRDM13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM13 BINDING SITE, designated SEQ ID:22256, to the nucleotide sequence of VGAM1951 RNA, herein designated VGAM RNA, also designated SEQ ID:4662.

[65802] Another function of VGAM1951 is therefore inhibition of PR Domain Containing 13 (PRDM13, Accession NM\_021620). Accordingly, utilities of VGAM1951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM13. LOC143308 (Accession XM\_096411) is another VGAM1951 host target gene. LOC143308 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC143308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC143308 BINDING SITE, designated SEQ ID:40347, to the nucleotide sequence of VGAM1951 RNA, herein designated VGAM RNA, also designated SEQ ID:4662.

[65803] Another function of VGAM1951 is therefore inhibition of LOC143308 (Accession XM\_096411). Accordingly, utilities of VGAM1951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143308. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1952 (VGAM1952) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65804] VGAM1952 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1952 was detected is described hereinabove with reference to Figs. 1–8.

[65805] VGAM1952 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Paramyxovirus 6. VGAM1952 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[65806] VGAM1952 gene encodes a VGAM1952 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1952 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1952 precursor RNA is designated SEQ ID:1938, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1938 is located at position 12992 relative to the genome of Avian Paramyxovirus 6.

[65807] VGAM1952 precursor RNA folds onto itself, forming VGAM1952 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65808] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1952 folded precursor RNA into VGAM1952 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1952 RNA is designated SEQ ID:4663, and is provided hereinbelow with reference to the sequence listing part.

[65809] VGAM1952 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1952 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1952 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65810] VGAM1952 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1952 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1952 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-



quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1952 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1952 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65811] The complementary binding of VGAM1952 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1952 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1952 host target RNA into VGAM1952 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65812] It is appreciated that VGAM1952 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1952 host target genes. The mRNA of each one of this plurality of VGAM1952 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1952 RNA, herein designated VGAM RNA, and which when bound by VGAM1952 RNA causes inhibition of translation of respective one or more VGAM1952 host target proteins.

[65813] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1952 gene, herein designated VGAM GENE, on one or more VGAM1952 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65814] It is yet further appreciated that a function of VGAM1952 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of viral infection by Avian Paramyxovirus 6. Specific functions, and accordingly utilities, of VGAM1952 correlate with, and may be deduced from, the identity of the host target genes which VGAM1952 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65815] Nucleotide sequences of the VGAM1952 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1952 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1952 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1952 are further described hereinbelow with reference to Table 1.

[65816] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1952 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1952 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65817] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1952 gene, herein designated VGAM is inhibition of expression of VGAM1952 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1952 correlate with, and may be deduced from, the identity of the target genes which VGAM1952 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65818] Cytochrome P450, Subfamily VIIA (cholesterol 7 alpha-monooxygenase), Polypeptide 1 (CYP7A1, Accession NM\_000780) is a VGAM1952 host target gene. CYP7A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP7A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP7A1 BINDING SITE, designated SEQ ID:6422, to the nucleotide sequence of VGAM1952 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4663.

[65819] A function of VGAM1952 is therefore inhibition of Cytochrome P450, Subfamily VIIA (cholesterol 7 alpha-monooxygenase), Polypeptide 1 (CYP7A1, Accession NM\_000780), a gene which functions in cholesterol and bile acid metabolism . Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP7A1. The function of CYP7A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM414.F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM\_012300) is another VGAM1952 host target gene. FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FBXW1B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3, designated SEQ ID:14661, SEQ ID:27363 and SEQ ID:27373 respectively, to the nucleotide sequence of VGAM1952 RNA, herein designated VGAM RNA, also designated SEQ

ID:4663.

[65820] Another function of VGAM1952 is therefore inhibition of F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM\_012300), a gene which somehow is involved in the process of neuronal cell differentiation or brain development. Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXW1B. The function of FBXW1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Inositol 1,4,5-triphosphate Receptor, Type 2 (ITPR2, Accession NM\_002223) is another VGAM1952 host target gene. ITPR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR2 BINDING SITE, designated SEQ ID:7991, to the nucleotide sequence of VGAM1952 RNA, herein designated VGAM RNA, also designated SEQ ID:4663.

[65821] Another function of VGAM1952 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 2 (ITPR2, Ac-

cession NM\_002223). Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR2. FLJ10508 (Accession NM\_018118) is another VGAM1952 host target gene. FLJ10508 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10508 BINDING SITE, designated SEQ ID:19890, to the nucleotide sequence of VGAM1952 RNA, herein designated VGAM RNA, also designated SEQ ID:4663.

[65822] Another function of VGAM1952 is therefore inhibition of FLJ10508 (Accession NM\_018118). Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10508. FLJ13110 (Accession NM\_022912) is another VGAM1952 host target gene. FLJ13110 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ13110 BINDING SITE, designated SEQ ID:23221, to the nucleotide sequence of VGAM1952 RNA, herein designated VGAM RNA, also designated SEQ ID:4663.

[65823] Another function of VGAM1952 is therefore inhibition of FLJ13110 (Accession NM\_022912). Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13110. Interleukin 17D (IL17D, Accession NM\_138284) is another VGAM1952 host target gene. IL17D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL17D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL17D BINDING SITE, designated SEQ ID:28701, to the nucleotide sequence of VGAM1952 RNA, herein designated VGAM RNA, also designated SEQ ID:4663.

[65824] Another function of VGAM1952 is therefore inhibition of Interleukin 17D (IL17D, Accession NM\_138284). Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL17D. KIAA1600 (Accession XM\_049351) is an-



other VGAM1952 host target gene. KIAA1600 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1600 BINDING SITE, designated SEQ ID:35393, to the nucleotide sequence of VGAM1952 RNA, herein designated VGAM RNA, also designated SEQ ID:4663.

[65825] Another function of VGAM1952 is therefore inhibition of KIAA1600 (Accession XM\_049351). Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1600. Target of Myb1-like 1 (chicken) (TOM1L1, Accession NM\_005486) is another VGAM1952 host target gene. TOM1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOM1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOM1L1 BINDING SITE, designated SEQ ID:11983, to the nucleotide sequence of VGAM1952 RNA, herein designated VGAM RNA, also designated SEQ

ID:4663.

[65826] Another function of VGAM1952 is therefore inhibition of Target of Myb1-like 1 (chicken) (TOM1L1, Accession NM\_005486). Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOM1L1. LOC221143 (Accession XM\_167986) is another VGAM1952 host target gene. LOC221143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221143 BINDING SITE, designated SEQ ID:44941, to the nucleotide sequence of VGAM1952 RNA, herein designated VGAM RNA, also designated SEQ ID:4663.

[65827] Another function of VGAM1952 is therefore inhibition of LOC221143 (Accession XM\_167986). Accordingly, utilities of VGAM1952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221143. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1953 (VGAM1953) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65828] VGAM1953 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1953 was detected is described hereinabove with reference to Figs. 1–8.

[65829] VGAM1953 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Paramyxovirus 6. VGAM1953 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65830] VGAM1953 gene encodes a VGAM1953 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1953 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1953 precursor RNA is designated SEQ ID:1939, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1939 is located at position 3760 relative to the genome of Avian Paramyxovirus 6.

[65831] VGAM1953 precursor RNA folds onto itself, forming VGAM1953 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65832] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1953 folded precursor RNA into VGAM1953 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1953 RNA is designated SEQ ID:4664, and is provided hereinbelow with reference to the sequence listing part.

[65833] VGAM1953 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1953 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1953 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[65834] VGAM1953 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1953 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1953 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1953 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1953 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65835] The complementary binding of VGAM1953 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1953 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1953 host target RNA into VGAM1953 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65836] It is appreciated that VGAM1953 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1953 host target genes. The mRNA of each one of this plurality of VGAM1953 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1953 RNA, herein designated VGAM RNA, and which when bound by VGAM1953 RNA causes inhibition of translation of respective one or more VGAM1953 host target proteins.

[65837] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1953 gene, herein designated VGAM GENE, on one or more VGAM1953 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65838] It is yet further appreciated that a function of VGAM1953 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1953 include diagnosis, prevention and treatment of viral infection by Avian Paramyxovirus 6. Specific functions, and accordingly utilities, of VGAM1953 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1953 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65839] Nucleotide sequences of the VGAM1953 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1953 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1953 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1953 are further described hereinbelow with reference to Table 1.

[65840] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1953 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1953 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65841] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1953 gene, herein designated VGAM is inhibition of expression of VGAM1953 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1953 correlate with, and may be deduced from, the identity of the target genes which VGAM1953



binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65842] Glucose-6-phosphate Dehydrogenase (G6PD, Accession NM\_000402) is a VGAM1953 host target gene. G6PD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by G6PD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G6PD BINDING SITE, designated SEQ ID:5978, to the nucleotide sequence of VGAM1953 RNA, herein designated VGAM RNA, also designated SEQ ID:4664.

[65843] A function of VGAM1953 is therefore inhibition of Glucose-6-phosphate Dehydrogenase (G6PD, Accession NM\_000402), a gene which produces pentose sugars for nucleic acid synthesis and main producer of nadph reducing power. Accordingly, utilities of VGAM1953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G6PD. The function of G6PD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1027.PR Domain Containing 2, with ZNF Domain (PRDM2, Accession

NM\_012231) is another VGAM1953 host target gene. PRDM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRDM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM2 BINDING SITE, designated SEQ ID:14531, to the nucleotide sequence of VGAM1953 RNA, herein designated VGAM RNA, also designated SEQ ID:4664.

[65844] Another function of VGAM1953 is therefore inhibition of PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM\_012231), a gene which plays a role in transcriptional regulation during neuronal differentiation and pathogenesis of retinoblastoma. Accordingly, utilities of VGAM1953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM2. The function of PRDM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120.FLJ20257 (Accession NM\_019606) is another VGAM1953 host target gene. FLJ20257 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by FLJ20257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20257 BINDING SITE, designated SEQ ID:21221, to the nucleotide sequence of VGAM1953 RNA, herein designated VGAM RNA, also designated SEQ ID:4664.

[65845] Another function of VGAM1953 is therefore inhibition of FLJ20257 (Accession NM\_019606). Accordingly, utilities of VGAM1953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20257. KIAA1030 (Accession XM\_167789) is another VGAM1953 host target gene. KIAA1030 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1030, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1030 BINDING SITE, designated SEQ ID:44818, to the nucleotide sequence of VGAM1953 RNA, herein designated VGAM RNA, also designated SEQ ID:4664.

[65846] Another function of VGAM1953 is therefore inhibition of KIAA1030 (Accession XM\_167789). Accordingly, utilities

of VGAM1953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1030. Phosphodiesterase 8A (PDE8A, Accession XM\_031443) is another VGAM1953 host target gene. PDE8A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE8A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE8A BINDING SITE, designated SEQ ID:31379, to the nucleotide sequence of VGAM1953 RNA, herein designated VGAM RNA, also designated SEQ ID:4664.

[65847] Another function of VGAM1953 is therefore inhibition of Phosphodiesterase 8A (PDE8A, Accession XM\_031443). Accordingly, utilities of VGAM1953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE8A. Paternally Expressed 10 (PEG10, Accession NM\_015068) is another VGAM1953 host target gene. PEG10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEG10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEG10 BINDING SITE, designated SEQ ID:17428, to the nucleotide sequence of VGAM1953 RNA, herein designated VGAM RNA, also designated SEQ ID:4664.

[65848] Another function of VGAM1953 is therefore inhibition of Paternally Expressed 10 (PEG10, Accession NM\_015068). Accordingly, utilities of VGAM1953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEG10. LOC204084 (Accession XM\_115181) is another VGAM1953 host target gene. LOC204084 BINDING SITE1 and LOC204084 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC204084, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204084 BINDING SITE1 and LOC204084 BINDING SITE2, designated SEQ ID:43088 and SEQ ID:43087 respectively, to the nucleotide sequence of VGAM1953 RNA, herein designated VGAM RNA, also designated SEQ ID:4664.

[65849] Another function of VGAM1953 is therefore inhibition of

LOC204084 (Accession XM\_115181). Accordingly, utilities of VGAM1953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204084. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1954 (VGAM1954) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65850] VGAM1954 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1954 was detected is described hereinabove with reference to Figs. 1-8.

[65851] VGAM1954 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Paramyxovirus 6. VGAM1954 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65852] VGAM1954 gene encodes a VGAM1954 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1954 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1954 precursor RNA is designated SEQ ID:1940, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1940 is located at position 6741 relative to the genome of Avian Paramyxovirus 6.

- [65853] VGAM1954 precursor RNA folds onto itself, forming VGAM1954 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [65854] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1954 folded precursor RNA into VGAM1954 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide se-

quence of VGAM1954 RNA is designated SEQ ID:4665, and is provided hereinbelow with reference to the sequence listing part.

[65855] VGAM1954 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1954 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1954 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65856] VGAM1954 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1954 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1954 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is



meant as an illustration only, and is not meant to be limiting – VGAM1954 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1954 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[65857] The complementary binding of VGAM1954 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1954 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1954 host target RNA into VGAM1954 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65858] It is appreciated that VGAM1954 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1954 host target genes. The mRNA of each one of this plurality of VGAM1954 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1954 RNA, herein designated VGAM RNA, and which when bound by VGAM1954 RNA causes inhibition of translation of respective one or more VGAM1954 host target proteins.

[65859] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1954 gene, herein designated VGAM GENE, on one or more VGAM1954 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65860] It is yet further appreciated that a function of VGAM1954

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1954 include diagnosis, prevention and treatment of viral infection by Avian Paramyxovirus 6. Specific functions, and accordingly utilities, of VGAM1954 correlate with, and may be deduced from, the identity of the host target genes which VGAM1954 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65861] Nucleotide sequences of the VGAM1954 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1954 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1954 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1954 are further described hereinbelow with reference to Table 1.

[65862] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1954 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1954 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65863] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1954 gene, herein designated VGAM is inhibition of expression of VGAM1954 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1954 correlate with, and may be deduced from, the identity of the target genes which VGAM1954 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65864] COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM\_004376) is a VGAM1954 host target gene. COX15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX15 BINDING SITE, designated SEQ ID:10599, to the nucleotide sequence of VGAM1954 RNA, herein designated VGAM RNA, also designated SEQ ID:4665.

[65865] A function of VGAM1954 is therefore inhibition of COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM\_004376). Accordingly, utilities of VGAM1954 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with COX15. Tumor Necrosis Factor Receptor Superfamily, Member 9 (TNFRSF9, Accession NM\_001561) is another VGAM1954 host target gene. TNFRSF9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF9 BINDING SITE, designated SEQ ID:7287, to the nucleotide sequence of VGAM1954 RNA, herein designated VGAM RNA, also designated SEQ ID:4665.

[65866] Another function of VGAM1954 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 9 (TNFRSF9, Accession NM\_001561), a gene which inhibits proliferation of activated T lymphocytes. Accordingly, utilities of VGAM1954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF9. The function of TNFRSF9 has been established by previous studies. Schwarz et al. (1996) reported that ILA inhibits proliferation of activated T lymphocytes and induces programmed cell death. Loo et al. (1997) reported that, unlike its mouse counterpart, human 4-1BB

binds only to its ligand, TNFSF9, and not to extracellular matrix proteins such as laminin (see OMIM Ref. No. 150240). The authors attributed this species distinction to sequence differences in the N-terminal laminin-homologous domain of human 4-1BB.

[65867] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[65868] Loo, D. T.; Chalupny, N. J.; Bajorath, J.; Shuford, W. W.; Mittler, R. S.; Aruffo, A. : Analysis of 4-1BBL and laminin binding to murine 4-1BB, a member of the tumor necrosis factor receptor superfamily, and comparison with human 4-1BB. J. Biol. Chem. 272: 6448-6456, 1997. ; and

[65869] Schwarz, H.; Arden, K.; Lotz, M. : CD137, a member of the tumor necrosis factor receptor family, is located on chromosome 1p36, in a cluster of related genes, and colocalizes with sever.

[65870] Further studies establishing the function and utilities of TNFRSF9 are found in John Hopkins OMIM database record ID 602250, and in cited publications numbered 6205-6210 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.

Chromosome 20 Open Reading Frame 121

(C20orf121, Accession NM\_024331) is another VGAM1954 host target gene. C20orf121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf121 BINDING SITE, designated SEQ ID:23627, to the nucleotide sequence of VGAM1954 RNA, herein designated VGAM RNA, also designated SEQ ID:4665.

[65871] Another function of VGAM1954 is therefore inhibition of Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM\_024331). Accordingly, utilities of VGAM1954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf121. Ligand of Numb-protein X (LNX, Accession NM\_032622) is another VGAM1954 host target gene. LNX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LNX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LNX BINDING SITE, designated SEQ ID:26337, to the nu-

cleotide sequence of VGAM1954 RNA, herein designated VGAM RNA, also designated SEQ ID:4665.

[65872] Another function of VGAM1954 is therefore inhibition of Ligand of Numb–protein X (LNX, Accession NM\_032622). Accordingly, utilities of VGAM1954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LNX. LOC202181 (Accession XM\_114456) is another VGAM1954 host target gene. LOC202181 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC202181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202181 BINDING SITE, designated SEQ ID:42967, to the nucleotide sequence of VGAM1954 RNA, herein designated VGAM RNA, also designated SEQ ID:4665.

[65873] Another function of VGAM1954 is therefore inhibition of LOC202181 (Accession XM\_114456). Accordingly, utilities of VGAM1954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202181. LOC93206 (Accession XM\_049838) is another VGAM1954 host target gene. LOC93206 BINDING



SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93206, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93206 BINDING SITE, designated SEQ ID:35515, to the nucleotide sequence of VGAM1954 RNA, herein designated VGAM RNA, also designated SEQ ID:4665.

[65874] Another function of VGAM1954 is therefore inhibition of LOC93206 (Accession XM\_049838). Accordingly, utilities of VGAM1954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93206. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1955 (VGAM1955) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65875] VGAM1955 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1955 was detected is described hereinabove with reference to Figs. 1–8.

[65876] VGAM1955 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1955 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65877] VGAM1955 gene encodes a VGAM1955 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1955 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1955 precursor RNA is designated SEQ ID:1941, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1941 is located at position 6373 relative to the genome of Macaca Mulatta Rhadinovirus.

[65878] VGAM1955 precursor RNA folds onto itself, forming VGAM1955 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[65879] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1955 folded precursor RNA into VGAM1955 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1955 RNA is designated SEQ ID:4666, and is provided hereinbelow with reference to the sequence listing part.

[65880] VGAM1955 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1955 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1955 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65881] VGAM1955 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1955 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1955 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1955 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1955 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65882] The complementary binding of VGAM1955 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1955 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1955 host target RNA into VGAM1955 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65883] It is appreciated that VGAM1955 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1955 host target genes. The mRNA of each one of this plurality of VGAM1955 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1955 RNA, herein designated VGAM RNA, and which when bound by VGAM1955 RNA causes inhibition of translation of respective one or more VGAM1955 host target proteins.

[65884] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1955 gene, herein designated VGAM GENE, on one or more VGAM1955 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65885] It is yet further appreciated that a function of VGAM1955 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1955 correlate with, and may be deduced from, the identity of the host target genes which VGAM1955 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65886] Nucleotide sequences of the VGAM1955 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1955 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1955 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1955 are further described hereinbelow with reference to Table 1.

[65887] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1955 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1955 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65888] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1955 gene, herein designated VGAM is inhibition of expression of VGAM1955 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1955 correlate with, and may be deduced from, the identity of the target genes which VGAM1955 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65889] Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession NM\_000489) is a VGAM1955 host target gene. ATRX BINDING SITE1 and ATRX BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ATRX, corresponding to HOST TARGET binding

sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATRX BINDING SITE1 and ATRX BINDING SITE2, designated SEQ ID:6098 and SEQ ID:28687 respectively, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65890] A function of VGAM1955 is therefore inhibition of Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession NM\_000489). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATRX. Ceroid-lipofuscinosis, Neuronal 5 (CLN5, Accession NM\_006493) is another VGAM1955 host target gene. CLN5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN5 BINDING SITE, designated SEQ ID:13231, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.



[65891] Another function of VGAM1955 is therefore inhibition of Ceroid–lipofuscinosis, Neuronal 5 (CLN5, Accession NM\_006493). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN5. Calponin 2 (CNN2, Accession NM\_004368) is another VGAM1955 host target gene. CNN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNN2 BINDING SITE, designated SEQ ID:10583, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65892] Another function of VGAM1955 is therefore inhibition of Calponin 2 (CNN2, Accession NM\_004368), a gene which may be involved in the structural organization and/or anchorage of actin filaments. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNN2. The function of CNN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM1498.Chondroitin Sulfate Proteoglycan 3 (neurocan) (CSPG3, Accession NM\_004386) is another VGAM1955 host target gene. CSPG3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSPG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSPG3 BINDING SITE, designated SEQ ID:10616, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65893] Another function of VGAM1955 is therefore inhibition of Chondroitin Sulfate Proteoglycan 3 (neurocan) (CSPG3, Accession NM\_004386), a gene which may play a role in modulating cell adhesion and migration. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSPG3. The function of CSPG3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM634.DMC1 Dosage Suppressor of Mck1 Homolog, Meiosis-specific Homologous Recombination (yeast) (DMC1, Accession NM\_007068) is another

VGAM1955 host target gene. DMC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DMC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMC1 BINDING SITE, designated SEQ ID:13934, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65894] Another function of VGAM1955 is therefore inhibition of DMC1 Dosage Suppressor of Mck1 Homolog, Meiosis-specific Homologous Recombination (yeast) (DMC1, Accession NM\_007068). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMC1. DnaJ (Hsp40) Homolog, Subfamily B, Member 9 (DNAJB9, Accession NM\_012328) is another VGAM1955 host target gene. DNAJB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJB9 BINDING SITE, designated SEQ

ID:14719, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65895] Another function of VGAM1955 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily B, Member 9 (DNAJB9, Accession NM\_012328). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJB9. Dual Specificity Phosphatase 6 (DUSP6, Accession XM\_038308) is another VGAM1955 host target gene. DUSP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DUSP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP6 BINDING SITE, designated SEQ ID:32809, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65896] Another function of VGAM1955 is therefore inhibition of Dual Specificity Phosphatase 6 (DUSP6, Accession XM\_038308), a gene which inactivates map kinases. Accordingly, utilities of VGAM1955 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with DUSP6. The function of DUSP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1763.DXS1283E

(Accession XM\_047871) is another VGAM1955 host target gene. DXS1283E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DXS1283E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DXS1283E BINDING SITE, designated SEQ ID:35063, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65897] Another function of VGAM1955 is therefore inhibition of DXS1283E (Accession XM\_047871). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DXS1283E. F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM\_012300) is another VGAM1955 host target gene. FBXW1B BINDING SITE1 through FBXW1B BINDING SITE6 are HOST TARGET binding sites found in

untranslated regions of mRNA encoded by FBXW1B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXW1B BINDING SITE1 through FBXW1B BINDING SITE6, designated SEQ ID:14665, SEQ ID:27381, SEQ ID:27377, SEQ ID:14669, SEQ ID:27367 and SEQ ID:27371 respectively, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65898] Another function of VGAM1955 is therefore inhibition of F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM\_012300), a gene which somehow is involved in the process of neuronal cell differentiation or brain development. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXW1B. The function of FBXW1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Glyoxalase I (GLO1, Accession NM\_006708) is another VGAM1955 host target gene. GLO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by GLO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLO1 BINDING SITE, designated SEQ ID:13529, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65899] Another function of VGAM1955 is therefore inhibition of Glyoxalase I (GLO1, Accession NM\_006708), a gene which converts methylglyoxal and glutathione to S-lactoylglutathione. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLO1. The function of GLO1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM786. Insulin Receptor Substrate 2 (IRS2, Accession XM\_007095) is another VGAM1955 host target gene. IRS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRS2 BINDING

SITE, designated SEQ ID:30032, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65900] Another function of VGAM1955 is therefore inhibition of Insulin Receptor Substrate 2 (IRS2, Accession XM\_007095), a gene which may mediate the control of various cellular processes by insulin. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRS2. The function of IRS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1217. Junctional Adhesion Molecule 3 (JAM3, Accession NM\_032801) is another VGAM1955 host target gene. JAM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JAM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAM3 BINDING SITE, designated SEQ ID:26554, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65901] Another function of VGAM1955 is therefore inhibition of



Junctional Adhesion Molecule 3 (JAM3, Accession NM\_032801), a gene which is a member of the junctional adhesion molecule protein family. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAM3. The function of JAM3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Low Density Lipoprotein Receptor-related Protein 8, Apolipoprotein E Receptor (LRP8, Accession NM\_004631) is another VGAM1955 host target gene. LRP8 BINDING SITE1 and LRP8 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LRP8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP8 BINDING SITE1 and LRP8 BINDING SITE2, designated SEQ ID:11007 and SEQ ID:27131 respectively, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65902] Another function of VGAM1955 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 8,

Apolipoprotein E Receptor (LRP8, Accession NM\_004631), a gene which binds vldl and transports it into cells by endocytosis. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP8. The function of LRP8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Neural Precursor Cell Expressed, Developmentally Down-regulated 4 (NEDD4, Accession XM\_046129) is another VGAM1955 host target gene. NEDD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEDD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEDD4 BINDING SITE, designated SEQ ID:34694, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65903] Another function of VGAM1955 is therefore inhibition of Neural Precursor Cell Expressed, Developmentally Down-regulated 4 (NEDD4, Accession XM\_046129), a gene which ubiquitinates regulatory proteins involved in transcription.

Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEDD4. The function of NEDD4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM209. Protocadherin Alpha 9 (PCDHA9, Accession NM\_014005) is another VGAM1955 host target gene. PCDHA9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE, designated SEQ ID:15217, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65904] Another function of VGAM1955 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM\_014005), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9

and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Polycystic Kidney Disease (polycystin) and REJ (sperm receptor for egg jelly homolog, sea urchin)-like (PKDREJ, Accession NM\_006071) is another VGAM1955 host target gene. PKDREJ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKDREJ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKDREJ BINDING SITE, designated SEQ ID:12716, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65905] Another function of VGAM1955 is therefore inhibition of Polycystic Kidney Disease (polycystin) and REJ (sperm receptor for egg jelly homolog, sea urchin)-like (PKDREJ, Accession NM\_006071), a gene which may intervene in fertilization. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKDREJ. The function of PKDREJ and its association with various diseases and clinical

cal conditions, has been established by previous studies, as described hereinabove with reference to VGAM641. Prion Protein (p27–30) (Creutzfeld–Jakob disease, Gerstmann–Strausler–Scheinker syndrome, fatal familial insomnia) (PRNP, Accession NM\_000311) is another VGAM1955 host target gene. PRNP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRNP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRNP BINDING SITE, designated SEQ ID:5848, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65906] Another function of VGAM1955 is therefore inhibition of Prion Protein (p27–30) (Creutzfeld–Jakob disease, Gerstmann–Strausler–Scheinker syndrome, fatal familial insomnia) (PRNP, Accession NM\_000311), a gene which the function of prp is not known. prp is encoded in the host genome and is expressed both in normal and infected cells. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRNP. The function of PRNP and its

association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM669.RAB1A, Member RAS Oncogene Family (RAB1A, Accession XM\_046674) is another VGAM1955 host target gene. RAB1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB1A BINDING SITE, designated SEQ ID:34788, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65907] Another function of VGAM1955 is therefore inhibition of RAB1A, Member RAS Oncogene Family (RAB1A, Accession XM\_046674), a gene which is involved in vesicle transport. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB1A. The function of RAB1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433.RNA (guanine-7-) Methyltransferase (RNMT, Accession

NM\_003799) is another VGAM1955 host target gene.

RNMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNMT BINDING SITE, designated SEQ ID:9894, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65908] Another function of VGAM1955 is therefore inhibition of RNA (guanine-7-) Methyltransferase (RNMT, Accession NM\_003799), a gene which catalyzes the methylation of GpppN- at the guanine N7 position. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNMT. The function of RNMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178.RNTRE (Accession NM\_014688) is another VGAM1955 host target gene. RNTRE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNTRE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNTRE BINDING SITE, designated SEQ ID:16191, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65909] Another function of VGAM1955 is therefore inhibition of RNTRE (Accession NM\_014688), a gene which may be involved in cell proliferation. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNTRE. The function of RNTRE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM379.Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 7 (SLC4A7, Accession NM\_003615) is another VGAM1955 host target gene. SLC4A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC4A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A7 BINDING SITE, designated SEQ ID:9675, to the nucleotide sequence of VGAM1955 RNA,



herein designated VGAM RNA, also designated SEQ ID:4666.

[65910] Another function of VGAM1955 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 7 (SLC4A7, Accession NM\_003615), a gene which mediates the coupled movement of sodium and bicarbonate ions across the plasma membrane. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A7. The function of SLC4A7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM66. Sclerosteosis (SOST, Accession NM\_025237) is another VGAM1955 host target gene. SOST BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOST, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOST BINDING SITE, designated SEQ ID:24919, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65911] Another function of VGAM1955 is therefore inhibition of Sclerosteosis (SOST, Accession NM\_025237). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOST. TAP Binding Protein (tapasin) (TAPBP, Accession NM\_003190) is another VGAM1955 host target gene. TAPBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAPBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAPBP BINDING SITE, designated SEQ ID:9185, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65912] Another function of VGAM1955 is therefore inhibition of TAP Binding Protein (tapasin) (TAPBP, Accession NM\_003190), a gene which is involved in MHC class I-restricted antigen processing. Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAPBP. The function of TAPBP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM122.TOX (Accession NM\_014729) is another VGAM1955 host target gene. TOX BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOX BINDING SITE, designated SEQ ID:16326, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65913] Another function of VGAM1955 is therefore inhibition of TOX (Accession NM\_014729). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOX. 5T4 (Accession NM\_006670) is another VGAM1955 host target gene. 5T4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by 5T4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of 5T4 BINDING SITE, designated SEQ ID:13486, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ

ID:4666.

[65914] Another function of VGAM1955 is therefore inhibition of 5T4 (Accession NM\_006670). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with 5T4. Abhydrolase Domain Containing 3 (ABHD3, Accession NM\_138340) is another VGAM1955 host target gene. ABHD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABHD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABHD3 BINDING SITE, designated SEQ ID:28741, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65915] Another function of VGAM1955 is therefore inhibition of Abhydrolase Domain Containing 3 (ABHD3, Accession NM\_138340). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABHD3. Acetyl-Coenzyme A Synthetase 2 (AMP forming)-like (ACAS2L, Accession XM\_042770) is another VGAM1955 host target gene.

ACAS2L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACAS2L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACAS2L BINDING SITE, designated SEQ ID:33767, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65916] Another function of VGAM1955 is therefore inhibition of Acetyl-Coenzyme A Synthetase 2 (AMP forming)-like (ACAS2L, Accession XM\_042770). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACAS2L. Rho GTPase Activating Protein 5 (ARHGAP5, Accession XM\_085082) is another VGAM1955 host target gene. ARHGAP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGAP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP5 BINDING SITE, designated SEQ ID:37819, to the nucleotide sequence of VGAM1955

RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65917] Another function of VGAM1955 is therefore inhibition of Rho GTPase Activating Protein 5 (ARHGAP5, Accession XM\_085082). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP5. BM046 (Accession NM\_018460) is another VGAM1955 host target gene. BM046 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BM046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BM046 BINDING SITE, designated SEQ ID:20532, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65918] Another function of VGAM1955 is therefore inhibition of BM046 (Accession NM\_018460). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BM046. BPES (Accession NM\_023067) is another VGAM1955 host target gene. BPES BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by BPES, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BPES BINDING SITE, designated SEQ ID:23324, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65919] Another function of VGAM1955 is therefore inhibition of BPES (Accession NM\_023067). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BPES. DJ473B4 (Accession NM\_019556) is another VGAM1955 host target gene. DJ473B4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DJ473B4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ473B4 BINDING SITE, designated SEQ ID:21212, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65920] Another function of VGAM1955 is therefore inhibition of

DJ473B4 (Accession NM\_019556). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ473B4. DJ971N18.2 (Accession NM\_021156) is another VGAM1955 host target gene. DJ971N18.2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ971N18.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ971N18.2 BINDING SITE, designated SEQ ID:22136, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65921] Another function of VGAM1955 is therefore inhibition of DJ971N18.2 (Accession NM\_021156). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ971N18.2. DKFZP434E2318 (Accession NM\_032138) is another VGAM1955 host target gene. DKFZP434E2318 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434E2318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING



SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434E2318 BINDING SITE, designated SEQ ID:25818, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65922] Another function of VGAM1955 is therefore inhibition of DKFZP434E2318 (Accession NM\_032138). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434E2318. DKFZP434I1735 (Accession XM\_113763) is another VGAM1955 host target gene. DKFZP434I1735 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434I1735, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I1735 BINDING SITE, designated SEQ ID:42423, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65923] Another function of VGAM1955 is therefore inhibition of DKFZP434I1735 (Accession XM\_113763). Accordingly, utilities of VGAM1955 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP434I1735. DKFZP434P0721 (Accession XM\_033181) is another VGAM1955 host target gene. DKFZP434P0721 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P0721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P0721 BINDING SITE, designated SEQ ID:31870, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65924] Another function of VGAM1955 is therefore inhibition of DKFZP434P0721 (Accession XM\_033181). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0721. DKFZP586M0622 (Accession NM\_015583) is another VGAM1955 host target gene. DKFZP586M0622 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP586M0622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of DKFZP586M0622 BINDING SITE, designated SEQ ID:17848, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65925] Another function of VGAM1955 is therefore inhibition of DKFZP586M0622 (Accession NM\_015583). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586M0622. EFA6R (Accession NM\_015310) is another VGAM1955 host target gene. EFA6R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFA6R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFA6R BINDING SITE, designated SEQ ID:17629, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65926] Another function of VGAM1955 is therefore inhibition of EFA6R (Accession NM\_015310). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFA6R. ERp44 (Accession XM\_088476) is another VGAM1955 host

target gene. ERp44 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ERp44, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERp44 BINDING SITE, designated SEQ ID:39727, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65927] Another function of VGAM1955 is therefore inhibition of ERp44 (Accession XM\_088476). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERp44. Formin Homology 2 Domain Containing 2 (FHOD2, Accession XM\_057927) is another VGAM1955 host target gene. FHOD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FHOD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHOD2 BINDING SITE, designated SEQ ID:36555, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ

ID:4666.

[65928] Another function of VGAM1955 is therefore inhibition of Formin Homology 2 Domain Containing 2 (FHOD2, Accession XM\_057927). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHOD2. FLJ10008 (Accession NM\_017970) is another VGAM1955 host target gene. FLJ10008 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10008, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10008 BINDING SITE, designated SEQ ID:19693, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65929] Another function of VGAM1955 is therefore inhibition of FLJ10008 (Accession NM\_017970). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10008. FLJ12587 (Accession NM\_022480) is another VGAM1955 host target gene. FLJ12587 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ12587, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12587 BINDING SITE, designated SEQ ID:22850, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65930] Another function of VGAM1955 is therefore inhibition of FLJ12587 (Accession NM\_022480). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12587. FLJ13340 (Accession NM\_057175) is another VGAM1955 host target gene. FLJ13340 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13340 BINDING SITE, designated SEQ ID:27705, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65931] Another function of VGAM1955 is therefore inhibition of FLJ13340 (Accession NM\_057175). Accordingly, utilities of

VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13340. FLJ20276 (Accession NM\_017738) is another VGAM1955 host target gene. FLJ20276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20276 BINDING SITE, designated SEQ ID:19328, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65932] Another function of VGAM1955 is therefore inhibition of FLJ20276 (Accession NM\_017738). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20276. FLJ20294 (Accession NM\_017749) is another VGAM1955 host target gene. FLJ20294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20294

BINDING SITE, designated SEQ ID:19346, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65933] Another function of VGAM1955 is therefore inhibition of FLJ20294 (Accession NM\_017749). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20294. GT650 (Accession NM\_052851) is another VGAM1955 host target gene. GT650 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GT650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GT650 BINDING SITE, designated SEQ ID:27435, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65934] Another function of VGAM1955 is therefore inhibition of GT650 (Accession NM\_052851). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GT650. KIAA0447 (Accession XM\_049733) is another VGAM1955 host target gene. KIAA0447 BINDING SITE is HOST TARGET



binding site found in the 3' untranslated region of mRNA encoded by KIAA0447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0447 BINDING SITE, designated SEQ ID:35496, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65935] Another function of VGAM1955 is therefore inhibition of KIAA0447 (Accession XM\_049733). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0447. KIAA0753 (Accession NM\_014804) is another VGAM1955 host target gene. KIAA0753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0753 BINDING SITE, designated SEQ ID:16738, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65936] Another function of VGAM1955 is therefore inhibition of

KIAA0753 (Accession NM\_014804). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0753. KIAA0820 (Accession XM\_044463) is another VGAM1955 host target gene. KIAA0820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0820 BINDING SITE, designated SEQ ID:34223, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65937] Another function of VGAM1955 is therefore inhibition of KIAA0820 (Accession XM\_044463). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0820. KIAA0836 (Accession XM\_035390) is another VGAM1955 host target gene. KIAA0836 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0836 BINDING SITE, designated SEQ ID:32246, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65938] Another function of VGAM1955 is therefore inhibition of KIAA0836 (Accession XM\_035390). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0836. KIAA1005 (Accession XM\_051197) is another VGAM1955 host target gene. KIAA1005 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1005, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1005 BINDING SITE, designated SEQ ID:35780, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65939] Another function of VGAM1955 is therefore inhibition of KIAA1005 (Accession XM\_051197). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1005. KIAA1041 (Accession NM\_014947) is another

VGAM1955 host target gene. KIAA1041 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1041, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1041 BINDING SITE, designated SEQ ID:17268, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65940] Another function of VGAM1955 is therefore inhibition of KIAA1041 (Accession NM\_014947). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1041. KIAA1468 (Accession XM\_166289) is another VGAM1955 host target gene. KIAA1468 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1468 BINDING SITE, designated SEQ ID:44101, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65941] Another function of VGAM1955 is therefore inhibition of KIAA1468 (Accession XM\_166289). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1468. KIAA1546 (Accession XM\_042301) is another VGAM1955 host target gene. KIAA1546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1546 BINDING SITE, designated SEQ ID:33714, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65942] Another function of VGAM1955 is therefore inhibition of KIAA1546 (Accession XM\_042301). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1546. KIAA1727 (Accession XM\_034262) is another VGAM1955 host target gene. KIAA1727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1727, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1727 BINDING SITE, designated SEQ ID:32039, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65943] Another function of VGAM1955 is therefore inhibition of KIAA1727 (Accession XM\_034262). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1727. KIAA1764 (Accession XM\_045086) is another VGAM1955 host target gene. KIAA1764 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1764, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1764 BINDING SITE, designated SEQ ID:34355, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65944] Another function of VGAM1955 is therefore inhibition of KIAA1764 (Accession XM\_045086). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1764. KIAA1765 (Accession XM\_047355) is another VGAM1955 host target gene. KIAA1765 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1765, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1765 BINDING SITE, designated SEQ ID:34958, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65945] Another function of VGAM1955 is therefore inhibition of KIAA1765 (Accession XM\_047355). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1765. Kelch-like 8 (Drosophila) (KLHL8, Accession XM\_031735) is another VGAM1955 host target gene. KLHL8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL8 BINDING SITE, designated SEQ ID:31477, to the nucleotide sequence of VGAM1955 RNA,

herein designated VGAM RNA, also designated SEQ ID:4666.

[65946] Another function of VGAM1955 is therefore inhibition of Kelch-like 8 (Drosophila) (KLHL8, Accession XM\_031735). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL8. LIN-28 (Accession NM\_024674) is another VGAM1955 host target gene. LIN-28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIN-28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIN-28 BINDING SITE, designated SEQ ID:23981, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65947] Another function of VGAM1955 is therefore inhibition of LIN-28 (Accession NM\_024674). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIN-28. MGC12466 (Accession XM\_086336) is another VGAM1955 host target gene. MGC12466 BINDING SITE is HOST TAR-



GET binding site found in the 3' untranslated region of mRNA encoded by MGC12466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12466 BINDING SITE, designated SEQ ID:38611, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65948] Another function of VGAM1955 is therefore inhibition of MGC12466 (Accession XM\_086336). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12466. MGC14859 (Accession XM\_030295) is another VGAM1955 host target gene. MGC14859 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC14859, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14859 BINDING SITE, designated SEQ ID:31007, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65949] Another function of VGAM1955 is therefore inhibition of

MGC14859 (Accession XM\_030295). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14859. MGC23937 (Accession NM\_145052) is another VGAM1955 host target gene. MGC23937 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC23937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC23937 BINDING SITE, designated SEQ ID:29683, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65950] Another function of VGAM1955 is therefore inhibition of MGC23937 (Accession NM\_145052). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC23937. MGC29898 (Accession NM\_145048) is another VGAM1955 host target gene. MGC29898 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC29898, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of MGC29898 BINDING SITE, designated SEQ ID:29680, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65951] Another function of VGAM1955 is therefore inhibition of MGC29898 (Accession NM\_145048). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC29898. Nudix (nucleoside diphosphate linked moiety X)-type Motif 13 (NUDT13, Accession XM\_032512) is another VGAM1955 host target gene. NUDT13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUDT13 BINDING SITE, designated SEQ ID:31663, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65952] Another function of VGAM1955 is therefore inhibition of Nudix (nucleoside diphosphate linked moiety X)-type Motif 13 (NUDT13, Accession XM\_032512). Accordingly, utilities of VGAM1955 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with NUDT13. OCT11 (Accession NM\_014352) is another VGAM1955 host target gene. OCT11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by OCT11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OCT11 BINDING SITE, designated SEQ ID:15681, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65953] Another function of VGAM1955 is therefore inhibition of OCT11 (Accession NM\_014352). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OCT11. Pellino Homolog 2 (Drosophila) (PELI2, Accession NM\_021255) is another VGAM1955 host target gene. PELI2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PELI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PELI2 BINDING SITE, designated SEQ ID:22230,

to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65954] Another function of VGAM1955 is therefore inhibition of Pellino Homolog 2 (Drosophila) (PELI2, Accession NM\_021255). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PELI2. RDC1 (Accession XM\_051522) is another VGAM1955 host target gene. RDC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RDC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDC1 BINDING SITE, designated SEQ ID:35848, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65955] Another function of VGAM1955 is therefore inhibition of RDC1 (Accession XM\_051522). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDC1. RES4-22 (Accession NM\_003704) is another VGAM1955 host target gene. RES4-22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by RES4-22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RES4-22 BINDING SITE, designated SEQ ID:9804, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65956] Another function of VGAM1955 is therefore inhibition of RES4-22 (Accession NM\_003704). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RES4-22. SE57-1 (Accession NM\_025214) is another VGAM1955 host target gene. SE57-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SE57-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SE57-1 BINDING SITE, designated SEQ ID:24894, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65957] Another function of VGAM1955 is therefore inhibition of SE57-1 (Accession NM\_025214). Accordingly, utilities of

VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SE57-1. SP192 (Accession NM\_021639) is another VGAM1955 host target gene. SP192 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SP192, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP192 BINDING SITE, designated SEQ ID:22300, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65958] Another function of VGAM1955 is therefore inhibition of SP192 (Accession NM\_021639). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP192. TBDN100 (Accession NM\_025085) is another VGAM1955 host target gene. TBDN100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBDN100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBDN100 BINDING SITE,

designated SEQ ID:24696, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65959] Another function of VGAM1955 is therefore inhibition of TBDN100 (Accession NM\_025085). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBDN100. Tumor Necrosis Factor Receptor Superfamily, Member 21 (TNFRSF21, Accession NM\_014452) is another VGAM1955 host target gene. TNFRSF21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF21 BINDING SITE, designated SEQ ID:15804, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65960] Another function of VGAM1955 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 21 (TNFRSF21, Accession NM\_014452). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



TNFRSF21. UBF-fl (Accession NM\_032828) is another VGAM1955 host target gene. UBF-fl BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBF-fl, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBF-fl BINDING SITE, designated SEQ ID:26603, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65961] Another function of VGAM1955 is therefore inhibition of UBF-fl (Accession NM\_032828). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBF-fl. Upstream Binding Protein 1 (LBP-1a) (UBP1, Accession NM\_014517) is another VGAM1955 host target gene. UB1 BINDING SITE1 and UB1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UB1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UB1 BINDING SITE1 and UB1 BINDING SITE2, designated SEQ ID:15849 and SEQ

ID:15848 respectively, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65962] Another function of VGAM1955 is therefore inhibition of Upstream Binding Protein 1 (LBP-1a) (UBP1, Accession NM\_014517). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBP1. ZFP106 (Accession NM\_022473) is another VGAM1955 host target gene. ZFP106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP106 BINDING SITE, designated SEQ ID:22838, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65963] Another function of VGAM1955 is therefore inhibition of ZFP106 (Accession NM\_022473). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP106. LOC120856 (Accession XM\_058509) is another

VGAM1955 host target gene. LOC120856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120856 BINDING SITE, designated SEQ ID:36631, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65964] Another function of VGAM1955 is therefore inhibition of LOC120856 (Accession XM\_058509). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120856. LOC122792 (Accession NM\_145251) is another VGAM1955 host target gene. LOC122792 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122792, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122792 BINDING SITE, designated SEQ ID:29765, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65965] Another function of VGAM1955 is therefore inhibition of LOC122792 (Accession NM\_145251). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122792. LOC130074 (Accession XM\_072228) is another VGAM1955 host target gene. LOC130074 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130074 BINDING SITE, designated SEQ ID:37473, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65966] Another function of VGAM1955 is therefore inhibition of LOC130074 (Accession XM\_072228). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130074. LOC135154 (Accession XM\_059752) is another VGAM1955 host target gene. LOC135154 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135154, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135154 BINDING SITE, designated SEQ ID:37091, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65967] Another function of VGAM1955 is therefore inhibition of LOC135154 (Accession XM\_059752). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135154. LOC146880 (Accession XM\_085627) is another VGAM1955 host target gene. LOC146880 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146880, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146880 BINDING SITE, designated SEQ ID:38260, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65968] Another function of VGAM1955 is therefore inhibition of LOC146880 (Accession XM\_085627). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC146880. LOC151963 (Accession XM\_087351) is another VGAM1955 host target gene. LOC151963 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151963, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151963 BINDING SITE, designated SEQ ID:39175, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65969] Another function of VGAM1955 is therefore inhibition of LOC151963 (Accession XM\_087351). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151963. LOC152580 (Accession XM\_098240) is another VGAM1955 host target gene. LOC152580 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152580 BINDING SITE, designated SEQ ID:41525, to the nucleotide sequence of VGAM1955 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4666.

[65970] Another function of VGAM1955 is therefore inhibition of LOC152580 (Accession XM\_098240). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152580. LOC158402 (Accession XM\_098936) is another VGAM1955 host target gene. LOC158402 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158402, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158402 BINDING SITE, designated SEQ ID:41979, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65971] Another function of VGAM1955 is therefore inhibition of LOC158402 (Accession XM\_098936). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158402. LOC168667 (Accession XM\_166592) is another VGAM1955 host target gene. LOC168667 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC168667, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168667 BINDING SITE, designated SEQ ID:44567, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65972] Another function of VGAM1955 is therefore inhibition of LOC168667 (Accession XM\_166592). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168667. LOC253263 (Accession XM\_173102) is another VGAM1955 host target gene. LOC253263 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253263 BINDING SITE, designated SEQ ID:46360, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65973] Another function of VGAM1955 is therefore inhibition of LOC253263 (Accession XM\_173102). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC253263. LOC90161 (Accession XM\_029551) is another VGAM1955 host target gene. LOC90161 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90161 BINDING SITE, designated SEQ ID:30904, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65974] Another function of VGAM1955 is therefore inhibition of LOC90161 (Accession XM\_029551). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90161. LOC90317 (Accession XM\_030892) is another VGAM1955 host target gene. LOC90317 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90317 BINDING SITE, designated SEQ ID:31209, to the

nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65975] Another function of VGAM1955 is therefore inhibition of LOC90317 (Accession XM\_030892). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90317. LOC91351 (Accession XM\_037817) is another VGAM1955 host target gene. LOC91351 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91351, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91351 BINDING SITE, designated SEQ ID:32697, to the nucleotide sequence of VGAM1955 RNA, herein designated VGAM RNA, also designated SEQ ID:4666.

[65976] Another function of VGAM1955 is therefore inhibition of LOC91351 (Accession XM\_037817). Accordingly, utilities of VGAM1955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91351. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1956 (VGAM1956) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[65977] VGAM1956 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1956 was detected is described hereinabove with reference to Figs. 1–8.

[65978] VGAM1956 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1956 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[65979] VGAM1956 gene encodes a VGAM1956 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1956 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1956 precursor RNA is designated SEQ ID:1942, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1942 is located at position 11662 relative to the genome of Macaca Mulatta Rhadinovirus.

[65980] VGAM1956 precursor RNA folds onto itself, forming VGAM1956 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[65981] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1956 folded precursor RNA into VGAM1956 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1956 RNA is designated SEQ ID:4667, and is provided hereinbelow with reference to the sequence listing part.

[65982] VGAM1956 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1956 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1956 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[65983] VGAM1956 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1956 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1956 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1956 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1956 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[65984] The complementary binding of VGAM1956 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1956 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1956 host target RNA into VGAM1956 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[65985] It is appreciated that VGAM1956 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1956 host target genes. The mRNA of each one of this plurality of VGAM1956 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1956 RNA, herein designated VGAM RNA, and which when bound by VGAM1956 RNA causes inhibition of translation of respective one or more VGAM1956 host target proteins.

[65986] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1956 gene, herein designated VGAM GENE, on one or more VGAM1956 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[65987] It is yet further appreciated that a function of VGAM1956 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1956 correlate with, and may be deduced from, the

identity of the host target genes which VGAM1956 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[65988] Nucleotide sequences of the VGAM1956 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1956 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1956 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1956 are further described hereinbelow with reference to Table 1.

[65989] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1956 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1956 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[65990] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1956 gene, herein designated VGAM is inhibition of expression of VGAM1956 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1956 correlate with, and may be deduced from, the identity of the target genes which VGAM1956



binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[65991] ATP-binding Cassette, Sub-family A (ABC1), Member 1 (ABCA1, Accession NM\_005502) is a VGAM1956 host target gene. ABCA1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ABCA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCA1 BINDING SITE, designated SEQ ID:12013, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[65992] A function of VGAM1956 is therefore inhibition of ATP-binding Cassette, Sub-family A (ABC1), Member 1 (ABCA1, Accession NM\_005502), a gene which camp-dependent and sulfonylurea-sensitive anion transporter. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCA1. The function of ABCA1 has been established by previous studies. By a PCR-based approach, Luciani et al. (1994) identified 2 novel mammalian members of the family of ATP-binding cassette (ABC) transporters desig-

nated ABC1 and ABC2 (OMIM Ref. No. 600047). They belong to a group of traffic ATPases encoded as a single multifunctional protein, such as CFTR (OMIM Ref. No. 602421) and P-glycoproteins (see OMIM Ref. No. 171050). Both ABC1 and ABC2 are large, internally symmetrical molecules that contain complete information for a functional 'channel-like' structure, a feature typical of the mammalian transporters at the plasma membrane. In both ABC1 and ABC2, the 2 halves of the molecules do not share extensive sequence similarity, apart from the nucleotide binding domains. This feature, shared with CFTR and with MRP1 (OMIM Ref. No. 158343), is in contrast with the high similarity shown by the 2 halves of P-glycoproteins. The finding argues against internal gene duplication as the event giving rise to the symmetric structure and favors the alternative hypothesis of the fusion of 2 independently evolved genes encoding the 2 halves. Santamarina-Fojo et al. (2000) found that the ABCA1 gene spans 149 kb and contains 50 exons. They identified 62 repetitive Alu sequences in the 49 introns. Comparative analysis of the mouse and human ABCA1 promoter sequences identified specific regulatory elements that are evolutionarily conserved. Pullinger et al.

(2000) analyzed the promoter region of ABCA1. They identified 7 putative SP1 (OMIM Ref. No. 189906)–binding sites, 4 sterol regulatory elements (SREs) similar to the SRE of the low density lipoprotein receptor (LDLR; 606945) promoter region, a CpG island, a possible weak TATA box, 2 distal CCAAT sequences, and binding sites for several other transcription factors.

[65993] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[65994] Luciani, M. F.; Denizot, F.; Savary, S.; Mattei, M. G.; Chimini, G. : Cloning of two novel ABC transporters mapping on human chromosome 9. *Genomics* 21: 150–159, 1994.  
; and

[65995] Santamarina–Fojo, S.; Peterson, K.; Knapper, C.; Qiu, Y.; Freeman, L.; Cheng, J.–F.; Osorio, J.; Remaley, A.; Yang, X.–P.; Haudenschield, C.; Prades, C.; Chimini, G.; Blackmon, E.; Franc.

[65996] Further studies establishing the function and utilities of ABCA1 are found in John Hopkins OMIM database record ID 600046, and in cited publications numbered 10228–9540, 10229, 10230–10231, 7375, 10232–10236, 10243, 10238–10240, 10244, 10249,

9586–7721, 1134 and 9587–7724 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Aspartate Beta-hydroxylase (ASPH, Accession NM\_032466) is another VGAM1956 host target gene. ASPH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ASPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASPH BINDING SITE, designated SEQ ID:26225, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[65997] Another function of VGAM1956 is therefore inhibition of Aspartate Beta-hydroxylase (ASPH, Accession NM\_032466), a gene which specifically hydroxylates the beta carbon of aspartic acid or asparagine residues in certain epidermal growth factor (EGF)-like domains of a number of proteins. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASPH. The function of ASPH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM47.BTB

and CNC Homology 1, Basic Leucine Zipper Transcription Factor 1 (BACH1, Accession NM\_001186) is another VGAM1956 host target gene. BACH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BACH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BACH1 BINDING SITE, designated SEQ ID:6859, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[65998] Another function of VGAM1956 is therefore inhibition of BTB and CNC Homology 1, Basic Leucine Zipper Transcription Factor 1 (BACH1, Accession NM\_001186), a gene which acts as repressor or activator, binds to nf- $\kappa$ B binding sites. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BACH1. The function of BACH1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM724. Breast Cancer 1, Early Onset (BRCA1, Accession NM\_007297) is another VGAM1956 host target gene. BRCA1 BINDING SITE

is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BRCA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRCA1 BINDING SITE, designated SEQ ID:14183, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[65999] Another function of VGAM1956 is therefore inhibition of Breast Cancer 1, Early Onset (BRCA1, Accession NM\_007297). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRCA1. Centrosomal Protein 2 (CEP2, Accession NM\_006779) is another VGAM1956 host target gene. CEP2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CEP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP2 BINDING SITE, designated SEQ ID:13651, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66000] Another function of VGAM1956 is therefore inhibition of Centrosomal Protein 2 (CEP2, Accession NM\_006779), a gene which interacts with TC10 and CDC42. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEP2. The function of CEP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM329. Carbamoyl-phosphate Synthetase 1, Mitochondrial (CPS1, Accession NM\_001875) is another VGAM1956 host target gene. CPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPS1 BINDING SITE, designated SEQ ID:7603, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66001] Another function of VGAM1956 is therefore inhibition of Carbamoyl-phosphate Synthetase 1, Mitochondrial (CPS1, Accession NM\_001875). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CPS1. DiGeorge Syndrome Critical Region Gene 2 (DGCR2, Accession NM\_005137) is another VGAM1956 host target gene. DGCR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGCR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGCR2 BINDING SITE, designated SEQ ID:11613, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66002] Another function of VGAM1956 is therefore inhibition of DiGeorge Syndrome Critical Region Gene 2 (DGCR2, Accession NM\_005137), a gene which could intervene in cell-cell or cell-matrix interactions. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGCR2. The function of DGCR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1485. Dihydropyrimidine Dehydrogenase (DPYD, Accession XM\_017469) is another VGAM1956



host target gene. DPYD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DPYD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPYD BINDING SITE, designated SEQ ID:30318, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66003] Another function of VGAM1956 is therefore inhibition of Dihydropyrimidine Dehydrogenase (DPYD, Accession XM\_017469). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYD. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM\_101395) is another VGAM1956 host target gene. DYRK1A BINDING SITE1 and DYRK1A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DYRK1A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE1 and DYRK1A BINDING SITE2,

designated SEQ ID:28164 and SEQ ID:28187 respectively, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66004] Another function of VGAM1956 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM\_101395), a gene which regulates cell proliferation and may be involved in brain development . Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK1A. The function of DYRK1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42.EH-domain Containing 2 (EHD2, Accession NM\_014601) is another VGAM1956 host target gene. EHD2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by EHD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EHD2 BINDING SITE, designated SEQ ID:15963, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66005] Another function of VGAM1956 is therefore inhibition of EH-domain Containing 2 (EHD2, Accession NM\_014601). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EHD2. ELK4, ETS-domain Protein (SRF accessory protein 1) (ELK4, Accession NM\_021795) is another VGAM1956 host target gene. ELK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELK4 BINDING SITE, designated SEQ ID:22351, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66006] Another function of VGAM1956 is therefore inhibition of ELK4, ETS-domain Protein (SRF accessory protein 1) (ELK4, Accession NM\_021795), a gene which may modulate SAP1 binding to DNA by interacting with its ETS domain. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELK4. The function of ELK4 has been established by previous studies. Regulation of gene expres-

sion often involves the interaction of transcription factors to form multicomponent complexes at promoter and enhancer elements. For example, transcriptional regulation of the FOS gene (OMIM Ref. No. 164810) in response to growth factor stimulation appears to involve a multicomponent complex at the serum response element (SRE). This complex contains the ubiquitous nuclear protein SRF together with a second protein, ternary complex factor (TCF), which cannot bind the SRE by itself. Dalton and Treisman (1992) employed a genetic screen using yeast to identify SAP1, an SRF accessory protein, which has DNA binding properties identical to those of TCF. Subsequently, they identified a related protein, SAP2 (OMIM Ref. No. 600247), by its cDNA sequence homology with the SAP1 cDNA. These proteins contain 3 regions of homology to a third protein, ELK1 (OMIM Ref. No. 311040), which also functions as an SRF accessory protein and is immunologically related to HeLa cell TCF. The SAP1, SAP2, and ELK1 mRNAs are ubiquitous. Shipley et al. (1994) used cDNA probes to isolate cosmid and phage clones harboring genes encoding SAP1 and SAP2. With these clones, they mapped the genes to 1q32 and 12q23, respectively, by fluorescence in situ hybridization. Giovane

et al. (1995) likewise mapped ELK4 to human 1q32 by in situ hybridization. By the same method, they mapped the mouse homolog to chromosome 1E3-G. Mo et al. (1998) determined the crystal structures of the conserved ETS domain of SAP1 bound to DNA sequences from the E74 and c-fos promoters. These structures revealed that a set of conserved residues contact a GGA core DNA sequence. Discrimination for sequences outside this core is mediated by DNA contacts from conserved and nonconserved protein residues and sequence-dependent DNA structural properties characteristic of A-form DNA structure. Modeling studies of a SAP1/SRF/DNA complex suggested that SRF may modulate SAP1 binding to DNA by interacting with its ETS domain.

[66007] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66008] Giovane, A.; Sobieszczuk, P.; Mignon, C.; Mattei, M.-G.; Wasylyk, B. : Locations of the ets subfamily members net, elk1, and sap1 (ELK3, ELK1, and ELK4) on three homologous regions of the mouse and human genomes. *Genomics* 29: 769-772, 1995. ; and

[66009] Mo, Y.; Vaessen, B.; Johnston, K.; Marmorstein, R. : Struc-

tures of SAP-1 bound to DNA targets from the E74 and c-fos promoters: insights into DNA sequence discrimination by Ets proteins.

[66010] Further studies establishing the function and utilities of ELK4 are found in John Hopkins OMIM database record ID 600246, and in cited publications numbered 791 and 8627-7920 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. E1A Binding Protein P300 (EP300, Accession NM\_001429) is another VGAM1956 host target gene. EP300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EP300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EP300 BINDING SITE, designated SEQ ID:7151, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66011] Another function of VGAM1956 is therefore inhibition of E1A Binding Protein P300 (EP300, Accession NM\_001429), a gene which may have a function in cell cycle regulation. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with EP300. The function of EP300 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. EphA2 (EPHA2, Accession NM\_004431) is another VGAM1956 host target gene. EPHA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA2 BINDING SITE, designated SEQ ID:10715, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66012] Another function of VGAM1956 is therefore inhibition of EphA2 (EPHA2, Accession NM\_004431), a gene which binds to ephrin-a1, -a3, -a4 and -a5. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA2. The function of EPHA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1289. Ellis Van Creveld Syndrome

(EVC, Accession NM\_014556) is another VGAM1956 host target gene. EVC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EVC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVC BINDING SITE, designated SEQ ID:15894, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66013] Another function of VGAM1956 is therefore inhibition of Ellis Van Creveld Syndrome (EVC, Accession NM\_014556). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVC. Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440) is another VGAM1956 host target gene. EXTL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EXTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL3 BINDING SITE, designated SEQ ID:7170, to the nucleotide sequence of



VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66014] Another function of VGAM1956 is therefore inhibition of Exostoses (multiple)-like 3 (EXTL3, Accession NM\_001440), a gene which is a member of the multiple exostoses gene family. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL3. The function of EXTL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome) (FGFR1, Accession NM\_023107) is another VGAM1956 host target gene. FGFR1 BINDING SITE1 through FGFR1 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGFR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGFR1 BINDING SITE1 through FGFR1 BINDING SITE6, designated SEQ ID:23362, SEQ ID:23366, SEQ ID:23373, SEQ ID:17979, SEQ ID:6208 and SEQ ID:23377 respectively, to the nucleotide se-

quence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66015] Another function of VGAM1956 is therefore inhibition of Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome) (FGFR1, Accession NM\_023107). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGFR1. Follistatin-like 3 (secreted glycoprotein) (FSTL3, Accession NM\_005860) is another VGAM1956 host target gene. FSTL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FSTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FSTL3 BINDING SITE, designated SEQ ID:12470, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66016] Another function of VGAM1956 is therefore inhibition of Follistatin-like 3 (secreted glycoprotein) (FSTL3, Accession NM\_005860), a gene which is a member of the follistatin-module-protein family. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FSTL3. The function of FSTL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Fucosyltransferase 5 (alpha (1,3) Fucosyltransferase) (FUT5, Accession NM\_002034) is another VGAM1956 host target gene. FUT5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT5 BINDING SITE, designated SEQ ID:7790, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66017] Another function of VGAM1956 is therefore inhibition of Fucosyltransferase 5 (alpha (1,3) Fucosyltransferase) (FUT5, Accession NM\_002034), a gene which may catalyze alpha-1,3 glycosidic linkages involved in the expression of vim-2, lewis x/ssea-1 and sialyl lewis x antigens. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT5. The function of FUT5 and its asso-

ciation with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1519. Fucosyltransferase 6 (alpha (1,3) Fucosyltransferase) (FUT6, Accession NM\_000150) is another VGAM1956 host target gene. FUT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT6 BINDING SITE, designated SEQ ID:5650, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66018] Another function of VGAM1956 is therefore inhibition of Fucosyltransferase 6 (alpha (1,3) Fucosyltransferase) (FUT6, Accession NM\_000150), a gene which is involved in the biosynthesis of the e-selectin ligand, sialyl-lewis x. FUT6 catalyzes the transfer of fucose from gdp-beta-fucose to alpha-2,3 sialylated substrates. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT6. The function of FUT6 and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM194. Glucose-6-phosphatase, Transport (glucose-6-phosphate) Protein 1 (G6PT1, Accession NM\_001467) is another VGAM1956 host target gene. G6PT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by G6PT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G6PT1 BINDING SITE, designated SEQ ID:7200, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66019] Another function of VGAM1956 is therefore inhibition of Glucose-6-phosphatase, Transport (glucose-6-phosphate) Protein 1 (G6PT1, Accession NM\_001467). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G6PT1. Guanine Nucleotide Binding Protein (G protein), Alpha 11 (Gq class) (GNA11, Accession XM\_072009) is another VGAM1956 host target gene. GNA11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNA11, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNA11 BINDING SITE, designated SEQ ID:37455, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66020] Another function of VGAM1956 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha 11 (Gq class) (GNA11, Accession XM\_072009), a gene which acts as an activator of phospholipase c. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNA11. The function of GNA11 has been established by previous studies. Strathmann and Simon (1991) described the Gna11 gene in the mouse. The human gene was cloned by Jiang et al. (1991) and found to be 359 amino acids long. Mouse Gna11 and Gna15 (OMIM Ref. No. 139314) are tandemly duplicated in a head-to-tail array. Davignon et al. (1996) showed that the upstream gene, Gna11, is ubiquitously expressed, whereas expression of the downstream gene, Gna15, is restricted to hematopoietic cells. There was no evidence for alternative splicing within the coding sequence of either gene. Animal

model experiments lend further support to the function of GNA11. Using gene targeting, Offermanns et al. (1998) generated Gna11-deficient mice that were viable and fertile with no apparent behavioral or morphologic defects. They bred Gnaq (OMIM Ref. No. 600998)-deficient mice with Gna11-deficient mice and observed gene dosage effects between Gnaq and Gna11. Embryos completely lacking both genes died in utero with heart malformations. Mice inheriting a single copy of either gene died within hours of birth with craniofacial and/or cardiac defects. Offermanns et al. (1998) concluded that at least 2 active alleles of these genes are required for extrauterine life. Genetic, morphologic, and pharmacologic analyses of intercross offspring inheriting different combinations of these 2 mutations indicated that Gnaq and Gna11 have overlapping functions in embryonic cardiomyocyte proliferation and craniofacial development.

[66021] It is appreciated that the abovementioned animal model for GNA11 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[66022] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [66023] Offermanns, S.; Zhao, L.-P.; Gohla, A.; Sarosi, I.; Simon, M. I.; Wilkie, T. M. : Embryonic cardiomyocyte hypoplasia and craniofacial defects in G-alpha-q/G-alpha-11-mutant mice. EMBO J. 17: 4304-4312, 1998. ; and
- [66024] Strathmann, M. P.; Simon, M. I. : G-alpha-12 and G-alpha-13 subunits define a fourth class of G protein alpha subunits. Proc. Nat. Acad. Sci. 88: 5582-5586, 1991.
- [66025] Further studies establishing the function and utilities of GNA11 are found in John Hopkins OMIM database record ID 139313, and in cited publications numbered 11937-1194 and 2186 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Guanine Nucleotide Binding Protein (G protein), Alpha 15 (Gq class) (GNA15, Accession XM\_009220) is another VGAM1956 host target gene. GNA15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNA15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNA15 BINDING SITE, designated SEQ ID:30105, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA,



also designated SEQ ID:4667.

[66026] Another function of VGAM1956 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha 15 (Gq class) (GNA15, Accession XM\_009220). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNA15. Glypican 6 (GPC6, Accession NM\_005708) is another VGAM1956 host target gene. GPC6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPC6 BINDING SITE, designated SEQ ID:12260, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66027] Another function of VGAM1956 is therefore inhibition of Glypican 6 (GPC6, Accession NM\_005708), a gene which may play a role in growth control and differentiation. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPC6. The function of GPC6 and its association with various diseases and clinical conditions, has

been established by previous studies, as described hereinabove with reference to VGAM247. Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM\_000838) is another VGAM1956 host target gene. GRM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM1 BINDING SITE, designated SEQ ID:6497, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66028] Another function of VGAM1956 is therefore inhibition of Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM\_000838), a gene which promotes phosphoinositide hydrolysis. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM1. The function of GRM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM786. Histamine Receptor H1 (HRH1, Accession NM\_000861) is another VGAM1956 host target gene.

HRH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRH1 BINDING SITE, designated SEQ ID:6526, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66029] Another function of VGAM1956 is therefore inhibition of Histamine Receptor H1 (HRH1, Accession NM\_000861), a gene which stimulates the synthesis of inositol phosphate. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRH1. The function of HRH1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM766. Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262) is another VGAM1956 host target gene. HS2ST1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HS2ST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of HS2ST1 BINDING SITE, designated SEQ ID:14575, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66030] Another function of VGAM1956 is therefore inhibition of Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM\_012262). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS2ST1. HTRA3 (Accession XM\_114416) is another VGAM1956 host target gene. HTRA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTRA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTRA3 BINDING SITE, designated SEQ ID:42943, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66031] Another function of VGAM1956 is therefore inhibition of HTRA3 (Accession XM\_114416). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTRA3.

Insulin Receptor Substrate 2 (IRS2, Accession XM\_007095) is another VGAM1956 host target gene. IRS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRS2 BINDING SITE, designated SEQ ID:30035, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66032] Another function of VGAM1956 is therefore inhibition of Insulin Receptor Substrate 2 (IRS2, Accession XM\_007095), a gene which may mediate the control of various cellular processes by insulin. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRS2. The function of IRS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1217. Integrin, Alpha M (complement component receptor 3, alpha; also known as CD11b (p170), Macrophage Antigen Alpha Polypeptide) (ITGAM, Accession NM\_000632) is another VGAM1956 host target gene.

ITGAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGAM BINDING SITE, designated SEQ ID:6249, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66033] Another function of VGAM1956 is therefore inhibition of Integrin, Alpha M (complement component receptor 3, alpha; also known as CD11b (p170), Macrophage Antigen Alpha Polypeptide) (ITGAM, Accession NM\_000632), a gene which is involved in various adhesive interactions of monocytes, macrophages and granulocytes as well as in mediating the uptake of complement-coated particles. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGAM. The function of ITGAM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1386. Lactate Dehydrogenase C (LDHC, Accession NM\_002301) is another VGAM1956 host target gene. LDHC BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LDHC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDHC BINDING SITE, designated SEQ ID:8092, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66034] Another function of VGAM1956 is therefore inhibition of Lactate Dehydrogenase C (LDHC, Accession NM\_002301). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDHC. Lysyl Oxidase-like 2 (LOXL2, Accession NM\_002318) is another VGAM1956 host target gene. LOXL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOXL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOXL2 BINDING SITE, designated SEQ ID:8134, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66035] Another function of VGAM1956 is therefore inhibition of Lysyl Oxidase-like 2 (LOXL2, Accession NM\_002318), a gene which may have roles in senescence and cell adhesion. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOXL2. The function of LOXL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM147. Myeloma Overexpressed Gene (in a subset of t(11;14) Positive Multiple Myelomas) (MYEOV, Accession NM\_138768) is another VGAM1956 host target gene. MYEOV BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MYEOV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYEOV BINDING SITE, designated SEQ ID:29002, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66036] Another function of VGAM1956 is therefore inhibition of Myeloma Overexpressed Gene (in a subset of t(11;14) Positive Multiple Myelomas) (MYEOV, Accession



NM\_138768), a gene which is encoded by MYELOMA OVEREXPRESSED GENE. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYEOV. The function of MYEOV and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM471. Pericentriolar Material 1 (PCM1, Accession NM\_006197) is another VGAM1956 host target gene. PCM1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PCM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCM1 BINDING SITE, designated SEQ ID:12870, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66037] Another function of VGAM1956 is therefore inhibition of Pericentriolar Material 1 (PCM1, Accession NM\_006197), a gene which appears to play a role in cytokinesis, cell shape, and specialized functions such as secretion and capping. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with PCM1. The function of PCM1 has been established by previous studies. Balczon et al. (1994) identified a 228-kD centrosome autoantigen designated PCM1 for pericentriolar material-1. In the course of investigating the region 8p22-p21.3, commonly involved in loss of heterozygosity in hepatocellular carcinomas, colorectal cancers, and non-small-cell lung cancers, Ohata et al. (1994) found a gene that was 100% identical to the nucleotide sequences of the cDNA for PCM1. The cosmid had previously been mapped to the 8p22-p21.3 region by fluorescence in situ hybridization and by pulsed field gel electrophoresis. Screening for rearrangements in Southern blots containing DNAs of a large number of cancers of the above-mentioned 3 types failed to demonstrate obvious rearrangements; however, a HindIII polymorphism in the PCM1 gene was found. The RET protooncogene (OMIM Ref. No. 164761) is often activated through somatic rearrangements in papillary thyroid carcinomas (OMIM Ref. No. 188550). Three main rearranged forms of RET have been described: RET/PTC1, in which the partner is called H4 (OMIM Ref. No. 601985) and RET/PTC3, in which the partner is called NCOA4 (OMIM Ref. No. 601984), both of which arise from a paracentric in-

version on 10q; and RET/PTC2, in which the partner is PRKAR1A (OMIM Ref. No. 188830), which originates from a 10;17 translocation. Corvi et al. (2000) identified a rearrangement involving the RET tyrosine kinase domain and the 5-prime portion of PCM1. FISH analysis confirmed the chromosomal localization of PCM1 on 8p22-p21. Immunohistochemistry using an antibody specific for the C-terminal portion of PCM1 showed that the protein level was drastically decreased and its subcellular localization altered in papillary thyroid tumor tissue with respect to normal thyroid.

[66038] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66039] Corvi, R.; Berger, N.; Balczon, R.; Romeo, G. : RET/PCM-1: a novel fusion gene in papillary thyroid carcinoma. *Oncogene* 19: 4236-4242, 2000. ; and

[66040] Ohata, H.; Fujiwara, Y.; Koyama, K.; Nakamura, Y. : Mapping of the human autoantigen pericentriolar material 1 (PCM1) gene to chromosome 8p21.3-p22. *Genomics* 24: 404-406, 1994.

[66041] Further studies establishing the function and utilities of PCM1 are found in John Hopkins OMIM database record ID

600299, and in cited publications numbered 158 and 1592–1593 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM\_006206) is another VGAM1956 host target gene. PDGFRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRA BINDING SITE, designated SEQ ID:12885, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66042] Another function of VGAM1956 is therefore inhibition of Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM\_006206), a gene which this receptor binds platelet-derived growth factor and has a tyrosine-protein kinase activity. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRA. The function of PDGFRA and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM117. Pim-1 Oncogene (PIM1, Accession XM\_165800) is another VGAM1956 host target gene. PIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIM1 BINDING SITE, designated SEQ ID:43757, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66043] Another function of VGAM1956 is therefore inhibition of Pim-1 Oncogene (PIM1, Accession XM\_165800), a gene which is a protooncogene. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIM1. The function of PIM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Perilipin (PLIN, Accession NM\_002666) is another VGAM1956 host target gene. PLIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLIN, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLIN BINDING SITE, designated SEQ ID:8536, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66044] Another function of VGAM1956 is therefore inhibition of Perilipin (PLIN, Accession NM\_002666). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLIN. POM (POM121 homolog, rat) and ZP3 Fusion (POMZP3, Accession NM\_012230) is another VGAM1956 host target gene. POMZP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by POMZP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POMZP3 BINDING SITE, designated SEQ ID:14529, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66045] Another function of VGAM1956 is therefore inhibition of POM (POM121 homolog, rat) and ZP3 Fusion (POMZP3,

Accession NM\_012230). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POMZP3. Paraoxonase 1 (PON1, Accession NM\_000446) is another VGAM1956 host target gene. PON1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PON1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PON1 BINDING SITE, designated SEQ ID:6033, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66046] Another function of VGAM1956 is therefore inhibition of Paraoxonase 1 (PON1, Accession NM\_000446), a gene which hydrolyzes the toxic metabolites of a variety of organophosphorus insecticides. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PON1. The function of PON1 has been established by previous studies. Two factors result in large individual variations in PON serum levels: a substrate-dependent activity polymorphism and large individual differences in PON protein

levels that are stable over time. Animal model studies indicated that PON activity levels are likely to play a major role in determining sensitivity to several organophosphate insecticides (Clendenning et al., 1996). The arg192 isoform (168820.0001) appears to be a risk factor in coronary artery disease. Serum paraoxonase is an esterase that is associated with high density lipoproteins (HDLs) in the plasma. It is involved in the detoxification of organophosphate insecticides such as parathion and chlorpyrifos. PON1 may also confer protection against coronary artery disease by destroying proinflammatory oxidized lipids present in oxidized low density lipoproteins (LDLs). To study the role of PON1 in vivo, Shih et al. (1998) created PON1-knockout mice by gene targeting. Compared with their wildtype littermates, PON1-deficient mice were extremely sensitive to the toxic effects of chlorpyrifos oxon, the activated form of chlorpyrifos, and were more sensitive to chlorpyrifos itself. HDLs isolated from PON1-deficient mice were unable to prevent LDL oxidation in a cocultured cell model of the artery wall, and both HDLs and LDLs isolated from PON1-knockout mice were more susceptible to oxidation by cocultured cells than were lipoproteins from wildtype littermates. When



fed on a high-fat, high-cholesterol diet, PON1-null mice were more susceptible to atherosclerosis than were their wildtype littermates.

[66047] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66048] Clendenning, J. B.; Humbert, R.; Green, E. D.; Wood, C.; Traver, D.; Furlong, C. E. : Structural organization of the human PON1 gene. *Genomics* 35: 586–589, 1996. ; and

[66049] Shih, D. M.; Gu, L.; Xia, Y.-R.; Navab, M.; Li, W.-F.; Hama, S.; Castellani, L. W.; Furlong, C. E.; Costa, L. G.; Fogelman, A. M.; Lusis, A. J. : Mice lacking serum paraoxonase are susceptible.

[66050] Further studies establishing the function and utilities of PON1 are found in John Hopkins OMIM database record ID 168820, and in cited publications numbered 11543–11555, 9, 2465–2486, 3780–249 and 3251–3252 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prospero-related Homeobox 1 (PROX1, Accession NM\_002763) is another VGAM1956 host target gene. PROX1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PROX1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROX1 BINDING SITE, designated SEQ ID:8651, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66051] Another function of VGAM1956 is therefore inhibition of Prospero-related Homeobox 1 (PROX1, Accession NM\_002763), a gene which may regulate gene expression and development of postmitotic undifferentiated young neurons. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROX1. The function of PROX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430. Prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy) (PSAP, Accession XM\_045140) is another VGAM1956 host target gene. PSAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of PSAP BINDING SITE, designated SEQ ID:34374, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66052] Another function of VGAM1956 is therefore inhibition of Prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy) (PSAP, Accession XM\_045140). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSAP. Prostaglandin-endoperoxide Synthase 2 (prostaglandin G/H synthase and cyclooxygenase) (PTGS2, Accession NM\_000963) is another VGAM1956 host target gene. PTGS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGS2 BINDING SITE, designated SEQ ID:6684, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66053] Another function of VGAM1956 is therefore inhibition of Prostaglandin-endoperoxide Synthase 2 (prostaglandin G/

H synthase and cyclooxygenase) (PTGS2, Accession NM\_000963), a gene which may have a role as a major mediator of inflammation and/or a role for prostanoid signaling in activity-dependent plasticity. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGS2. The function of PTGS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM292.

**RaIA Binding Protein 1** (RALBP1, Accession NM\_006788) is another VGAM1956 host target gene. RALBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RALBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RALBP1 BINDING SITE, designated SEQ ID:13665, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66054] Another function of VGAM1956 is therefore inhibition of RaIA Binding Protein 1 (RALBP1, Accession NM\_006788), a gene which plays a role in signal transduction and cat-

alyzes the transport of glutathione conjugates and xenobiotics. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RALBP1. The function of RALBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM345. Retinoic Acid Receptor, Alpha (RARA, Accession NM\_000964) is another VGAM1956 host target gene. RARA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RARA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RARA BINDING SITE, designated SEQ ID:6689, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66055] Another function of VGAM1956 is therefore inhibition of Retinoic Acid Receptor, Alpha (RARA, Accession NM\_000964). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RARA. RP42 (Accession NM\_020640) is another VGAM1956 host target gene.

RP42 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RP42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP42 BINDING SITE, designated SEQ ID:21802, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66056] Another function of VGAM1956 is therefore inhibition of RP42 (Accession NM\_020640), a gene which not clear yet. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP42. The function of RP42 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM47. Ribophorin II (RPN2, Accession NM\_002951) is another VGAM1956 host target gene. RPN2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RPN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPN2 BINDING SITE, designated SEQ

ID:8863, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66057] Another function of VGAM1956 is therefore inhibition of Ribophorin II (RPN2, Accession NM\_002951). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPN2. Spinocerebellar Ataxia 1 (olivopontocerebellar ataxia 1, autosomal dominant, ataxin 1) (SCA1, Accession NM\_000332) is another VGAM1956 host target gene. SCA1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SCA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCA1 BINDING SITE, designated SEQ ID:5880, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66058] Another function of VGAM1956 is therefore inhibition of Spinocerebellar Ataxia 1 (olivopontocerebellar ataxia 1, autosomal dominant, ataxin 1) (SCA1, Accession NM\_000332). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with SCA1. Syndecan 1 (SDC1, Accession NM\_002997) is another VGAM1956 host target gene. SDC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC1 BINDING SITE, designated SEQ ID:8888, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66059] Another function of VGAM1956 is therefore inhibition of Syndecan 1 (SDC1, Accession NM\_002997), a gene which mediates cell behaviors like cell adhesion, action of growth factors. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC1. The function of SDC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM534. Suppressor of Cytokine Signaling 5 (SOCS5, Accession NM\_014011) is another VGAM1956 host target gene. SOCS5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by



SOCS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOCS5 BINDING SITE, designated SEQ ID:15229, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66060] Another function of VGAM1956 is therefore inhibition of Suppressor of Cytokine Signaling 5 (SOCS5, Accession NM\_014011). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOCS5. SRY (sex determining region Y)-box 13 (SOX13, Accession NM\_005686) is another VGAM1956 host target gene. SOX13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOX13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX13 BINDING SITE, designated SEQ ID:12244, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66061] Another function of VGAM1956 is therefore inhibition of

SRY (sex determining region Y)-box 13 (SOX13, Accession NM\_005686). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOX13. SWAP70 (Accession XM\_049197) is another VGAM1956 host target gene.

SWAP70 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SWAP70, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SWAP70 BINDING SITE, designated SEQ ID:35349, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66062] Another function of VGAM1956 is therefore inhibition of SWAP70 (Accession XM\_049197), a gene which is involved not only in nuclear events but also in signaling in B-cell activation. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SWAP70. The function of SWAP70 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM1090.TAF6 RNA Polymerase II, TATA Box Binding Protein (TBP)–associated Factor, 80kDa (TAF6, Accession NM\_005641) is another VGAM1956 host target gene. TAF6 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TAF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF6 BINDING SITE, designated SEQ ID:12174, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66063] Another function of VGAM1956 is therefore inhibition of TAF6 RNA Polymerase II, TATA Box Binding Protein (TBP)–associated Factor, 80kDa (TAF6, Accession NM\_005641), a gene which plays a central role in mediating promoter responses to various activators and repressors. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF6. The function of TAF6 has been established by previous studies. TFIID is an essential general transcription factor (GTF) that binds stably to the TATA element of class II promoters and nucleates the assembly of other GTFs (e.g., 600519) and RNA polymerase

II (see OMIM Ref. No. 180660) into a functional preinitiation complex. It is composed of a highly conserved TATA-binding polypeptide (TBP; 600075) and tightly associated polypeptides called TBP-associated factors (TAFs), which are required for activator-dependent transcription. By screening a HeLa cell cDNA library with a *Drosophila* TAFII60 cDNA, Weinzierl et al. (1993) isolated cDNAs encoding TAF2E, which they called TAFII70. Sequence analysis revealed 3 distinct TAFII70 cDNAs, and the authors suggested that they corresponded to alternatively spliced transcripts. Southern blot analysis of human genomic DNA confirmed that TAFII70 is a single-copy gene. The 3 predicted TAFII70 proteins have 667, 677, and 726 amino acids; Weinzierl et al. (1993) chose a cDNA encoding the 677-amino acid isoform for further characterization. Recombinant TAFII70 bound weakly to TBP and tightly to TAFII250 (TAF2A; 313650), the largest subunit of TFIID. In the presence of TAFII70, TBP, and TAFII250, a stable ternary complex was formed. Independently, Hisatake et al. (1995) isolated a cDNA encoding TAF2E, which they called TAFII80, by screening a human placenta cDNA library with a 'best-guess' oligonucleotide based on a peptide sequence of TAFII80. Northern blot analysis detected

a 2.5-kb TAFII80 transcript. The predicted protein was identical to the deduced 677-amino acid protein of Weinzierl et al. (1993). TAFII80 is proline-rich overall and has a serine-, threonine-, and proline-rich region at its C terminus. The TAFII80 and Drosophila TAFII60 proteins share conserved regions of 50% and 64% sequence identity within their N-terminal and central sections, respectively. An N-terminal 55-amino acid segment of TAFII80 is 24% identical to a region of histone H4 that is believed to form part of the hydrophobic core of the histone octamer. TAFII80 from HeLa cell extracts had a molecular mass of 80 kD by Western blot analysis. Coimmunoprecipitation studies showed that TAFII80 interacted with TBP, TAFII250, TAFII31 (TAF2G; 600822), TAFII20 (TAF2J; 600773), TFIIE- $\alpha$  (GTF2E1; 189962), and TFIIF- $\alpha$  (GTF2F1; 189968); Hisatake et al. (1995) identified 3 distinct domains in TAFII80 that are involved in these interactions. TAFII80 did not interact with TAFII55 (TAF2F; 600573), TFIIB (GTF2B; 189963), TFIIE- $\beta$  (GTF2E2; 189964), or TFIIF- $\beta$  (GTF2F2; 189969).

[66064] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [66065] Hisatake, K.; Ohta, T.; Takada, R.; Guermah, M.; Horikoshi, M.; Nakatani, Y.; Roeder, R. G. : Evolutionary conservation of human TATA-binding-polypeptide-associated factors TAFII31 and TAFII80 and interactions of TAFII80 with other TAFs and with general transcription factors. Proc. Nat. Acad. Sci. 92: 8195–8199, 1995. ; and
- [66066] Weinzierl, R. O. J.; Ruppert, S.; Dynlacht, B. D.; Tanese, N.; Tjian, R. : Cloning and expression of Drosophila TAFII60 and human TAFII70 reveal conserved interactions with other subunit.
- [66067] Further studies establishing the function and utilities of TAF6 are found in John Hopkins OMIM database record ID 602955, and in cited publications numbered 8641–8643 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TNF Receptor-associated Factor 5 (TRAF5, Accession NM\_004619) is another VGAM1956 host target gene. TRAF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAF5 BINDING SITE, designated SEQ ID:10967, to the nucleotide se-

quence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66068] Another function of VGAM1956 is therefore inhibition of TNF Receptor-associated Factor 5 (TRAF5, Accession NM\_004619), a gene which Member of a family of proteins that interact with TNF receptors; binds the lymphotoxin beta receptor (LTBR). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF5. The function of TRAF5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM76.UV Radiation Resistance Associated Gene (UVRAG, Accession NM\_003369) is another VGAM1956 host target gene. UVRAG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by UVRAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UVRAG BINDING SITE, designated SEQ ID:9394, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66069] Another function of VGAM1956 is therefore inhibition of UV Radiation Resistance Associated Gene (UVRAG, Accession NM\_003369). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UVRAG. Vitamin D (1,25– dihydroxyvitamin D3) Receptor (VDR, Accession NM\_000376) is another VGAM1956 host target gene. VDR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VDR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VDR BINDING SITE, designated SEQ ID:5948, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66070] Another function of VGAM1956 is therefore inhibition of Vitamin D (1,25– dihydroxyvitamin D3) Receptor (VDR, Accession NM\_000376). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VDR. Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM\_133332) is another VGAM1956 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3 are



HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:28454, SEQ ID:28471 and SEQ ID:17190 respectively, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66071] Another function of VGAM1956 is therefore inhibition of Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM\_133332), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.ACF (Accession NM\_138932) is another VGAM1956 host target gene. ACF BINDING SITE1 and ACF BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ACF, corresponding to HOST TARGET binding sites such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACF BINDING SITE1 and ACF BINDING SITE2, designated SEQ ID:29059 and SEQ ID:15938 respectively, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66072] Another function of VGAM1956 is therefore inhibition of ACF (Accession NM\_138932). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACF. Bol, Boule-like (Drosophila) (BOLL, Accession NM\_033030) is another VGAM1956 host target gene. BOLL BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BOLL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BOLL BINDING SITE, designated SEQ ID:26922, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66073] Another function of VGAM1956 is therefore inhibition of Bol, Boule-like (Drosophila) (BOLL, Accession NM\_033030). Accordingly, utilities of VGAM1956 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with BOLL. Chromosome 22 Open Reading Frame 2 (C22orf2, Accession XM\_170492) is another VGAM1956 host target gene. C22orf2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C22orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf2 BINDING SITE, designated SEQ ID:45335, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66074] Another function of VGAM1956 is therefore inhibition of Chromosome 22 Open Reading Frame 2 (C22orf2, Accession XM\_170492). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf2. Chromobox Homolog 3 (HP1 gamma homolog, Drosophila) (CBX3, Accession NM\_007276) is another VGAM1956 host target gene. CBX3 BINDING SITE1 and CBX3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CBX3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II

or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBX3 BINDING SITE1 and CBX3 BINDING SITE2, designated SEQ ID:14142 and SEQ ID:18662 respectively, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66075] Another function of VGAM1956 is therefore inhibition of Chromobox Homolog 3 (HP1 gamma homolog, *Drosophila*) (CBX3, Accession NM\_007276). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX3. Chromatin Accessibility Complex 1 (CHRAC1, Accession NM\_017444) is another VGAM1956 host target gene. CHRAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRAC1 BINDING SITE, designated SEQ ID:18909, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66076] Another function of VGAM1956 is therefore inhibition of

Chromatin Accessibility Complex 1 (CHRAC1, Accession NM\_017444). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRAC1. Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM\_004273) is another VGAM1956 host target gene. CHST3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CHST3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST3 BINDING SITE, designated SEQ ID:10484, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66077] Another function of VGAM1956 is therefore inhibition of Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM\_004273). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST3. CRMP5 (Accession NM\_020134) is another VGAM1956 host target gene. CRMP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by CRMP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRMP5 BINDING SITE, designated SEQ ID:21334, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66078] Another function of VGAM1956 is therefore inhibition of CRMP5 (Accession NM\_020134). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRMP5. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 17, 72kDa (DDX17, Accession NM\_030881) is another VGAM1956 host target gene. DDX17 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DDX17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX17 BINDING SITE, designated SEQ ID:25156, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66079] Another function of VGAM1956 is therefore inhibition of

DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 17, 72kDa (DDX17, Accession NM\_030881). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX17. DKFZP434B044 (Accession NM\_031476) is another VGAM1956 host target gene. DKFZP434B044 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434B044, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434B044 BINDING SITE, designated SEQ ID:25554, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66080] Another function of VGAM1956 is therefore inhibition of DKFZP434B044 (Accession NM\_031476). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434B044. DKFZP762D096 (Accession XM\_037662) is another VGAM1956 host target gene. DKFZP762D096 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

DKFZP762D096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP762D096 BINDING SITE, designated SEQ ID:32666, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66081] Another function of VGAM1956 is therefore inhibition of DKFZP762D096 (Accession XM\_037662). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP762D096. Endothelial Cell-specific Molecule 1 (ESM1, Accession NM\_007036) is another VGAM1956 host target gene. ESM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESM1 BINDING SITE, designated SEQ ID:13913, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66082] Another function of VGAM1956 is therefore inhibition of



Endothelial Cell-specific Molecule 1 (ESM1, Accession NM\_007036). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESM1. FENS-1 (Accession NM\_020830) is another VGAM1956 host target gene. FENS-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FENS-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FENS-1 BINDING SITE, designated SEQ ID:21892, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66083] Another function of VGAM1956 is therefore inhibition of FENS-1 (Accession NM\_020830). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FENS-1. FLB6421 (Accession NM\_020119) is another VGAM1956 host target gene. FLB6421 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLB6421, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLB6421 BINDING SITE, designated SEQ ID:21302, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66084] Another function of VGAM1956 is therefore inhibition of FLB6421 (Accession NM\_020119). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLB6421. FLJ10521 (Accession NM\_018125) is another VGAM1956 host target gene. FLJ10521 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10521, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10521 BINDING SITE, designated SEQ ID:19912, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66085] Another function of VGAM1956 is therefore inhibition of FLJ10521 (Accession NM\_018125). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10521. FLJ10713 (Accession NM\_018189) is another VGAM1956 host target gene. FLJ10713 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10713 BINDING SITE, designated SEQ ID:20042, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66086] Another function of VGAM1956 is therefore inhibition of FLJ10713 (Accession NM\_018189). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10713. FLJ11164 (Accession NM\_018346) is another VGAM1956 host target gene. FLJ11164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11164 BINDING SITE, designated SEQ ID:20358, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM

RNA, also designated SEQ ID:4667.

[66087] Another function of VGAM1956 is therefore inhibition of FLJ11164 (Accession NM\_018346). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11164. FLJ11362 (Accession NM\_021946) is another VGAM1956 host target gene. FLJ11362 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11362 BINDING SITE, designated SEQ ID:22471, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66088] Another function of VGAM1956 is therefore inhibition of FLJ11362 (Accession NM\_021946). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11362. FLJ13197 (Accession NM\_024614) is another VGAM1956 host target gene. FLJ13197 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13197, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13197 BINDING SITE, designated SEQ ID:23872, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66089] Another function of VGAM1956 is therefore inhibition of FLJ13197 (Accession NM\_024614). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13197. FLJ13441 (Accession NM\_023924) is another VGAM1956 host target gene. FLJ13441 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13441 BINDING SITE, designated SEQ ID:23394, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66090] Another function of VGAM1956 is therefore inhibition of FLJ13441 (Accession NM\_023924). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ13441. FLJ13993 (Accession XM\_017638) is another VGAM1956 host target gene. FLJ13993 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13993, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13993 BINDING SITE, designated SEQ ID:30327, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66091] Another function of VGAM1956 is therefore inhibition of FLJ13993 (Accession XM\_017638). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13993. FLJ14075 (Accession NM\_024894) is another VGAM1956 host target gene. FLJ14075 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14075, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14075 BINDING SITE, designated SEQ ID:24376, to the nucleotide

sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66092] Another function of VGAM1956 is therefore inhibition of FLJ14075 (Accession NM\_024894). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14075. FLJ22548 (Accession NM\_022456) is another VGAM1956 host target gene. FLJ22548 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22548, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22548 BINDING SITE, designated SEQ ID:22794, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66093] Another function of VGAM1956 is therefore inhibition of FLJ22548 (Accession NM\_022456). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22548. FLJ23042 (Accession NM\_025157) is another VGAM1956 host target gene. FLJ23042 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ23042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23042 BINDING SITE, designated SEQ ID:24797, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66094] Another function of VGAM1956 is therefore inhibition of FLJ23042 (Accession NM\_025157). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23042. FLJ23360 (Accession NM\_023076) is another VGAM1956 host target gene. FLJ23360 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23360, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23360 BINDING SITE, designated SEQ ID:23336, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66095] Another function of VGAM1956 is therefore inhibition of FLJ23360 (Accession NM\_023076). Accordingly, utilities of



VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23360. FLJ30681 (Accession XM\_166291) is another VGAM1956 host target gene. FLJ30681 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30681 BINDING SITE, designated SEQ ID:44106, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66096] Another function of VGAM1956 is therefore inhibition of FLJ30681 (Accession XM\_166291). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30681. GMPPB (Accession XM\_171044) is another VGAM1956 host target gene. GMPPB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GMPPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GMPPB BINDING SITE,

designated SEQ ID:45817, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66097] Another function of VGAM1956 is therefore inhibition of GMPPB (Accession XM\_171044). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMPPB. GTP Binding Protein 2 (GTPBP2, Accession NM\_019096) is another VGAM1956 host target gene. GTPBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GTPBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTPBP2 BINDING SITE, designated SEQ ID:21173, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66098] Another function of VGAM1956 is therefore inhibition of GTP Binding Protein 2 (GTPBP2, Accession NM\_019096). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTPBP2. Hypermethylated In Cancer 2 (HIC2, Accession XM\_036937) is another VGAM1956

host target gene. HIC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC2 BINDING SITE, designated SEQ ID:32531, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66099] Another function of VGAM1956 is therefore inhibition of Hypermethylated In Cancer 2 (HIC2, Accession XM\_036937). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC2. HIG2 (Accession NM\_013332) is another VGAM1956 host target gene. HIG2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HIG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIG2 BINDING SITE, designated SEQ ID:14978, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66100] Another function of VGAM1956 is therefore inhibition of HIG2 (Accession NM\_013332). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIG2. HSC3 (Accession NM\_145174) is another VGAM1956 host target gene. HSC3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HSC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSC3 BINDING SITE, designated SEQ ID:29735, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66101] Another function of VGAM1956 is therefore inhibition of HSC3 (Accession NM\_145174). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSC3. HYPH (Accession XM\_170722) is another VGAM1956 host target gene. HYPH BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HYPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of HYPH BINDING SITE, designated SEQ ID:45483, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66102] Another function of VGAM1956 is therefore inhibition of HYPH (Accession XM\_170722). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HYPH. Interleukin 1 Family, Member 10 (theta) (IL1F10, Accession NM\_032556) is another VGAM1956 host target gene. IL1F10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IL1F10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1F10 BINDING SITE, designated SEQ ID:26284, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66103] Another function of VGAM1956 is therefore inhibition of Interleukin 1 Family, Member 10 (theta) (IL1F10, Accession NM\_032556). Accordingly, utilities of VGAM1956 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F10. KIAA0057 (Accession NM\_012288) is another VGAM1956 host target gene. KIAA0057 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0057 BINDING SITE, designated SEQ ID:14624, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66104] Another function of VGAM1956 is therefore inhibition of KIAA0057 (Accession NM\_012288). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0057. KIAA0317 (Accession NM\_014821) is another VGAM1956 host target gene. KIAA0317 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0317 BINDING SITE, designated SEQ ID:16796, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66105] Another function of VGAM1956 is therefore inhibition of KIAA0317 (Accession NM\_014821). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0317. KIAA0453 (Accession XM\_044546) is another VGAM1956 host target gene. KIAA0453 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0453 BINDING SITE, designated SEQ ID:34230, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66106] Another function of VGAM1956 is therefore inhibition of KIAA0453 (Accession XM\_044546). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0453. KIAA0618 (Accession NM\_014833) is another VGAM1956 host target gene. KIAA0618 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0618 BINDING SITE, designated SEQ ID:16837, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66107] Another function of VGAM1956 is therefore inhibition of KIAA0618 (Accession NM\_014833). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0618. KIAA0931 (Accession XM\_041191) is another VGAM1956 host target gene. KIAA0931 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0931, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0931 BINDING SITE, designated SEQ ID:33487, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66108] Another function of VGAM1956 is therefore inhibition of



KIAA0931 (Accession XM\_041191). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0931. KIAA1013 (Accession XM\_114303) is another VGAM1956 host target gene. KIAA1013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1013 BINDING SITE, designated SEQ ID:42859, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66109] Another function of VGAM1956 is therefore inhibition of KIAA1013 (Accession XM\_114303). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1013. KIAA1017 (Accession NM\_007216) is another VGAM1956 host target gene. KIAA1017 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1017 BINDING SITE, designated SEQ ID:14081, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66110] Another function of VGAM1956 is therefore inhibition of KIAA1017 (Accession NM\_007216). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1017. KIAA1193 (Accession XM\_041843) is another VGAM1956 host target gene. KIAA1193 BINDING SITE1 through KIAA1193 BINDING SITE21 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1193, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1193 BINDING SITE1 through KIAA1193 BINDING SITE21, designated SEQ ID:33591, SEQ ID:33606, SEQ ID:33604, SEQ ID:33605, SEQ ID:33600, SEQ ID:33603, SEQ ID:33590, SEQ ID:33592, SEQ ID:33594, SEQ ID:33597, SEQ ID:33586, SEQ ID:33587, SEQ ID:33588, SEQ ID:33589, SEQ ID:33595, SEQ ID:33596, SEQ ID:33593, SEQ ID:33601, SEQ ID:33602, SEQ ID:33598 and SEQ ID:33599 respec-

tively, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66111] Another function of VGAM1956 is therefore inhibition of KIAA1193 (Accession XM\_041843). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1193. KIAA1323 (Accession XM\_032146) is another VGAM1956 host target gene. KIAA1323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1323 BINDING SITE, designated SEQ ID:31568, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66112] Another function of VGAM1956 is therefore inhibition of KIAA1323 (Accession XM\_032146). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1323. KIAA1332 (Accession XM\_048774) is another VGAM1956 host target gene. KIAA1332 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1332 BINDING SITE, designated SEQ ID:35260, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66113] Another function of VGAM1956 is therefore inhibition of KIAA1332 (Accession XM\_048774). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1332. KIAA1450 (Accession XM\_038035) is another VGAM1956 host target gene. KIAA1450 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1450 BINDING SITE, designated SEQ ID:32749, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66114] Another function of VGAM1956 is therefore inhibition of

KIAA1450 (Accession XM\_038035). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1450. KIAA1627 (Accession XM\_087571) is another VGAM1956 host target gene. KIAA1627 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1627 BINDING SITE, designated SEQ ID:39344, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66115] Another function of VGAM1956 is therefore inhibition of KIAA1627 (Accession XM\_087571). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1627. KIAA1878 (Accession XM\_166256) is another VGAM1956 host target gene. KIAA1878 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1878, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1878 BINDING SITE, designated SEQ ID:44078, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66116] Another function of VGAM1956 is therefore inhibition of KIAA1878 (Accession XM\_166256). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1878. KIAA1900 (Accession XM\_055299) is another VGAM1956 host target gene. KIAA1900 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1900, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1900 BINDING SITE, designated SEQ ID:36259, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66117] Another function of VGAM1956 is therefore inhibition of KIAA1900 (Accession XM\_055299). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1900. KIAA1932 (Accession XM\_055900) is another

VGAM1956 host target gene. KIAA1932 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1932 BINDING SITE, designated SEQ ID:36350, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66118] Another function of VGAM1956 is therefore inhibition of KIAA1932 (Accession XM\_055900). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1932. KR18 (Accession NM\_033288) is another VGAM1956 host target gene. KR18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KR18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KR18 BINDING SITE, designated SEQ ID:27117, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66119] Another function of VGAM1956 is therefore inhibition of KR18 (Accession NM\_033288). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KR18. LIG-1 (Accession XM\_033712) is another VGAM1956 host target gene. LIG-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIG-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIG-1 BINDING SITE, designated SEQ ID:31953, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66120] Another function of VGAM1956 is therefore inhibition of LIG-1 (Accession XM\_033712). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIG-1. LIM Domain Kinase 2 (LIMK2, Accession NM\_005569) is another VGAM1956 host target gene. LIMK2 BINDING SITE1 and LIMK2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LIMK2, corresponding to HOST TARGET binding sites such



as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMK2 BINDING SITE1 and LIMK2 BINDING SITE2, designated SEQ ID:12096 and SEQ ID:18787 respectively, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66121] Another function of VGAM1956 is therefore inhibition of LIM Domain Kinase 2 (LIMK2, Accession NM\_005569). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMK2. Mitogen-activated Protein Kinase-activated Protein Kinase 2 (MAPKAPK2, Accession NM\_004759) is another VGAM1956 host target gene. MAPKAPK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPKAPK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPKAPK2 BINDING SITE, designated SEQ ID:11151, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66122] Another function of VGAM1956 is therefore inhibition of Mitogen-activated Protein Kinase-activated Protein Kinase 2 (MAPKAPK2, Accession NM\_004759). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPKAPK2. MGC13040 (Accession NM\_032930) is another VGAM1956 host target gene. MGC13040 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC13040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13040 BINDING SITE, designated SEQ ID:26755, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66123] Another function of VGAM1956 is therefore inhibition of MGC13040 (Accession NM\_032930). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13040. MGC14386 (Accession NM\_033544) is another VGAM1956 host target gene. MGC14386 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC14386, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14386 BINDING SITE, designated SEQ ID:27307, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66124] Another function of VGAM1956 is therefore inhibition of MGC14386 (Accession NM\_033544). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14386. MGC20481 (Accession XM\_031555) is another VGAM1956 host target gene. MGC20481 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20481 BINDING SITE, designated SEQ ID:31425, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66125] Another function of VGAM1956 is therefore inhibition of MGC20481 (Accession XM\_031555). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC20481. MGC2477 (Accession NM\_024099) is another VGAM1956 host target gene. MGC2477 BINDING SITE1 and MGC2477 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MGC2477, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2477 BINDING SITE1 and MGC2477 BINDING SITE2, designated SEQ ID:23544 and SEQ ID:23543 respectively, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66126] Another function of VGAM1956 is therefore inhibition of MGC2477 (Accession NM\_024099). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2477. MGC4342 (Accession NM\_024329) is another VGAM1956 host target gene. MGC4342 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC4342 BINDING SITE, designated SEQ ID:23625, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66127] Another function of VGAM1956 is therefore inhibition of MGC4342 (Accession NM\_024329). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4342. MGC4701 (Accession XM\_035378) is another VGAM1956 host target gene. MGC4701 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4701, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4701 BINDING SITE, designated SEQ ID:32242, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66128] Another function of VGAM1956 is therefore inhibition of MGC4701 (Accession XM\_035378). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4701. MGC9753 (Accession NM\_033419) is another

VGAM1956 host target gene. MGC9753 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC9753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC9753 BINDING SITE, designated SEQ ID:27243, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66129] Another function of VGAM1956 is therefore inhibition of MGC9753 (Accession NM\_033419). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC9753. MIC2 Like 1 (MIC2L1, Accession NM\_031462) is another VGAM1956 host target gene. MIC2L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIC2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIC2L1 BINDING SITE, designated SEQ ID:25494, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66130] Another function of VGAM1956 is therefore inhibition of MIC2 Like 1 (MIC2L1, Accession NM\_031462). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIC2L1. Neural Precursor Cell Expressed, Developmentally Down-regulated 5 (NEDD5, Accession NM\_004404) is another VGAM1956 host target gene. NEDD5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEDD5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEDD5 BINDING SITE, designated SEQ ID:10658, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66131] Another function of VGAM1956 is therefore inhibition of Neural Precursor Cell Expressed, Developmentally Down-regulated 5 (NEDD5, Accession NM\_004404). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEDD5. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM\_024607) is another

VGAM1956 host target gene. PPP1R3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R3B BINDING SITE, designated SEQ ID:23860, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66132] Another function of VGAM1956 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM\_024607). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R3B. PRO0971 (Accession NM\_018569) is another VGAM1956 host target gene. PRO0971 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0971 BINDING SITE, designated SEQ ID:20652, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM



RNA, also designated SEQ ID:4667.

[66133] Another function of VGAM1956 is therefore inhibition of PRO0971 (Accession NM\_018569). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0971. Rho-related BTB Domain Containing 2 (RHOBTB2, Accession XM\_027679) is another VGAM1956 host target gene. RHOBTB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RHOBTB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHOBTB2 BINDING SITE, designated SEQ ID:30562, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66134] Another function of VGAM1956 is therefore inhibition of Rho-related BTB Domain Containing 2 (RHOBTB2, Accession XM\_027679). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHOBTB2. RNA-binding Region (RNP1, RRM) Containing 1 (RNPC1, Accession NM\_017495) is another VGAM1956 host target gene.

RNPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNPC1 BINDING SITE, designated SEQ ID:18959, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66135] Another function of VGAM1956 is therefore inhibition of RNA-binding Region (RNP1, RRM) Containing 1 (RNPC1, Accession NM\_017495). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNPC1. Rpo1-2 (Accession NM\_019014) is another VGAM1956 host target gene. Rpo1-2 BINDING SITE1 and Rpo1-2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by Rpo1-2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rpo1-2 BINDING SITE1 and Rpo1-2 BINDING SITE2, designated SEQ ID:21105 and SEQ ID:25935 respectively, to the

nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66136] Another function of VGAM1956 is therefore inhibition of Rpo1-2 (Accession NM\_019014). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rpo1-2. Serologically Defined Colon Cancer Antigen 3 (SDCCAG3, Accession NM\_006643) is another VGAM1956 host target gene. SDCCAG3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDCCAG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDCCAG3 BINDING SITE, designated SEQ ID:13435, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66137] Another function of VGAM1956 is therefore inhibition of Serologically Defined Colon Cancer Antigen 3 (SDCCAG3, Accession NM\_006643). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDCCAG3. SEC61A1 (Accession NM\_013336) is another

VGAM1956 host target gene. SEC61A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC61A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC61A1 BINDING SITE, designated SEQ ID:14985, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66138] Another function of VGAM1956 is therefore inhibition of SEC61A1 (Accession NM\_013336). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC61A1. Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM\_006379) is another VGAM1956 host target gene. SEMA3C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEMA3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA3C BINDING SITE, designated SEQ ID:13074, to the nucleotide sequence of VGAM1956 RNA,

herein designated VGAM RNA, also designated SEQ ID:4667.

[66139] Another function of VGAM1956 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM\_006379). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA3C. SERP1 (Accession NM\_014445) is another VGAM1956 host target gene. SERP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERP1 BINDING SITE, designated SEQ ID:15797, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66140] Another function of VGAM1956 is therefore inhibition of SERP1 (Accession NM\_014445). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERP1. SHARP (Accession NM\_015001) is another VGAM1956 host

target gene. SHARP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SHARP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHARP BINDING SITE, designated SEQ ID:17368, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66141] Another function of VGAM1956 is therefore inhibition of SHARP (Accession NM\_015001). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHARP. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM\_018450) is another VGAM1956 host target gene. SMARCF1 BINDING SITE1 through SMARCF1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMARCF1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCF1 BINDING SITE1 through SMARCF1

BINDING SITE3, designated SEQ ID:20520, SEQ ID:12625 and SEQ ID:29163 respectively, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66142] Another function of VGAM1956 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM\_018450). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCF1. Synaptotagmin XIII (SYT13, Accession XM\_167880) is another VGAM1956 host target gene. SYT13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYT13 BINDING SITE, designated SEQ ID:44892, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66143] Another function of VGAM1956 is therefore inhibition of Synaptotagmin XIII (SYT13, Accession XM\_167880). Ac-

cordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYT13. SZF1 (Accession NM\_016089) is another VGAM1956 host target gene. SZF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SZF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SZF1 BINDING SITE, designated SEQ ID:18174, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66144] Another function of VGAM1956 is therefore inhibition of SZF1 (Accession NM\_016089). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SZF1. Testis Expressed Sequence 27 (TEX27, Accession NM\_021943) is another VGAM1956 host target gene. TEX27 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TEX27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-



quences of TEX27 BINDING SITE, designated SEQ ID:22461, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66145] Another function of VGAM1956 is therefore inhibition of Testis Expressed Sequence 27 (TEX27, Accession NM\_021943). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEX27. Tripartite Motif-containing 11 (TRIM11, Accession XM\_052974) is another VGAM1956 host target gene. TRIM11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM11 BINDING SITE, designated SEQ ID:36055, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66146] Another function of VGAM1956 is therefore inhibition of Tripartite Motif-containing 11 (TRIM11, Accession XM\_052974). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with TRIM11. Tripartite Motif-containing 38 (TRIM38, Accession NM\_006355) is another VGAM1956 host target gene. TRIM38 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM38, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM38 BINDING SITE, designated SEQ ID:13051, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66147] Another function of VGAM1956 is therefore inhibition of Tripartite Motif-containing 38 (TRIM38, Accession NM\_006355). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM38. Ubiquitin-conjugating Enzyme E2G 1 (UBC7 homolog, *C. elegans*) (UBE2G1, Accession NM\_003342) is another VGAM1956 host target gene. UBE2G1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of UBE2G1 BINDING SITE, designated SEQ ID:9350, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66148] Another function of VGAM1956 is therefore inhibition of Ubiquitin-conjugating Enzyme E2G 1 (UBC7 homolog, *C. elegans*) (UBE2G1, Accession NM\_003342). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2G1. ZFD25 (Accession NM\_016220) is another VGAM1956 host target gene. ZFD25 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZFD25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFD25 BINDING SITE, designated SEQ ID:18322, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66149] Another function of VGAM1956 is therefore inhibition of ZFD25 (Accession NM\_016220). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFD25.

Zinc Finger Protein 238 (ZNF238, Accession NM\_006352) is another VGAM1956 host target gene. ZNF238 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF238, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF238 BINDING SITE, designated SEQ ID:13045, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66150] Another function of VGAM1956 is therefore inhibition of Zinc Finger Protein 238 (ZNF238, Accession NM\_006352). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF238. LOC124460 (Accession XM\_071892) is another VGAM1956 host target gene. LOC124460 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124460 BINDING SITE, designated SEQ ID:37446, to the nucleotide sequence of

VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66151] Another function of VGAM1956 is therefore inhibition of LOC124460 (Accession XM\_071892). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124460. LOC130412 (Accession XM\_065708) is another VGAM1956 host target gene. LOC130412 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC130412, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130412 BINDING SITE, designated SEQ ID:37292, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66152] Another function of VGAM1956 is therefore inhibition of LOC130412 (Accession XM\_065708). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130412. LOC144486 (Accession XM\_096608) is another VGAM1956 host target gene. LOC144486 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC144486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144486 BINDING SITE, designated SEQ ID:40418, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66153] Another function of VGAM1956 is therefore inhibition of LOC144486 (Accession XM\_096608). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144486. LOC145082 (Accession XM\_096719) is another VGAM1956 host target gene. LOC145082 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145082 BINDING SITE, designated SEQ ID:40496, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66154] Another function of VGAM1956 is therefore inhibition of LOC145082 (Accession XM\_096719). Accordingly, utilities

of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145082. LOC145622 (Accession XM\_085186) is another VGAM1956 host target gene. LOC145622 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145622 BINDING SITE, designated SEQ ID:37914, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66155] Another function of VGAM1956 is therefore inhibition of LOC145622 (Accession XM\_085186). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145622. LOC145955 (Accession XM\_096912) is another VGAM1956 host target gene. LOC145955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145955 BINDING SITE, designated SEQ ID:40645, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66156] Another function of VGAM1956 is therefore inhibition of LOC145955 (Accession XM\_096912). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145955. LOC146146 (Accession XM\_085343) is another VGAM1956 host target gene. LOC146146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146146 BINDING SITE, designated SEQ ID:38072, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66157] Another function of VGAM1956 is therefore inhibition of LOC146146 (Accession XM\_085343). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146146. LOC146774 (Accession XM\_085584) is another VGAM1956 host target gene. LOC146774 BINDING



SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146774, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146774 BINDING SITE, designated SEQ ID:38236, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66158] Another function of VGAM1956 is therefore inhibition of LOC146774 (Accession XM\_085584). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146774. LOC148254 (Accession XM\_086121) is another VGAM1956 host target gene. LOC148254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148254 BINDING SITE, designated SEQ ID:38504, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66159] Another function of VGAM1956 is therefore inhibition of

LOC148254 (Accession XM\_086121). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148254. LOC148938 (Accession XM\_097555) is another VGAM1956 host target gene. LOC148938 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148938, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148938 BINDING SITE, designated SEQ ID:40928, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66160] Another function of VGAM1956 is therefore inhibition of LOC148938 (Accession XM\_097555). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148938. LOC149276 (Accession XM\_097621) is another VGAM1956 host target gene. LOC149276 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC149276 BINDING SITE, designated SEQ ID:40976, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66161] Another function of VGAM1956 is therefore inhibition of LOC149276 (Accession XM\_097621). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149276. LOC149705 (Accession XM\_097711) is another VGAM1956 host target gene. LOC149705 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149705 BINDING SITE, designated SEQ ID:41053, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66162] Another function of VGAM1956 is therefore inhibition of LOC149705 (Accession XM\_097711). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149705. LOC152137 (Accession XM\_087392) is an-

other VGAM1956 host target gene. LOC152137 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152137, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152137 BINDING SITE, designated SEQ ID:39222, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66163] Another function of VGAM1956 is therefore inhibition of LOC152137 (Accession XM\_087392). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152137. LOC153811 (Accession XM\_087779) is another VGAM1956 host target gene. LOC153811 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153811 BINDING SITE, designated SEQ ID:39418, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66164] Another function of VGAM1956 is therefore inhibition of LOC153811 (Accession XM\_087779). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153811. LOC157867 (Accession XM\_098831) is another VGAM1956 host target gene. LOC157867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157867 BINDING SITE, designated SEQ ID:41857, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66165] Another function of VGAM1956 is therefore inhibition of LOC157867 (Accession XM\_098831). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157867. LOC158308 (Accession XM\_098917) is another VGAM1956 host target gene. LOC158308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158308, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158308 BINDING SITE, designated SEQ ID:41941, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66166] Another function of VGAM1956 is therefore inhibition of LOC158308 (Accession XM\_098917). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158308. LOC159121 (Accession XM\_099028) is another VGAM1956 host target gene. LOC159121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC159121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159121 BINDING SITE, designated SEQ ID:42063, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66167] Another function of VGAM1956 is therefore inhibition of LOC159121 (Accession XM\_099028). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC159121. LOC162022 (Accession XM\_091293) is another VGAM1956 host target gene. LOC162022 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162022, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162022 BINDING SITE, designated SEQ ID:40043, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66168] Another function of VGAM1956 is therefore inhibition of LOC162022 (Accession XM\_091293). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162022. LOC169966 (Accession XM\_093010) is another VGAM1956 host target gene. LOC169966 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169966, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169966 BINDING SITE, designated SEQ ID:40166, to the nucleotide sequence of VGAM1956 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4667.

[66169] Another function of VGAM1956 is therefore inhibition of LOC169966 (Accession XM\_093010). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169966. LOC196500 (Accession XM\_113734) is another VGAM1956 host target gene. LOC196500 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196500, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196500 BINDING SITE, designated SEQ ID:42391, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66170] Another function of VGAM1956 is therefore inhibition of LOC196500 (Accession XM\_113734). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196500. LOC199688 (Accession XM\_117115) is another VGAM1956 host target gene. LOC199688 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199688, cor-



responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199688 BINDING SITE, designated SEQ ID:43230, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66171] Another function of VGAM1956 is therefore inhibition of LOC199688 (Accession XM\_117115). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199688. LOC199699 (Accession XM\_113990) is another VGAM1956 host target gene. LOC199699 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199699, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199699 BINDING SITE, designated SEQ ID:42596, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66172] Another function of VGAM1956 is therefore inhibition of LOC199699 (Accession XM\_113990). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC199699. LOC199796 (Accession XM\_058994) is another VGAM1956 host target gene. LOC199796 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC199796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199796 BINDING SITE, designated SEQ ID:36812, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66173] Another function of VGAM1956 is therefore inhibition of LOC199796 (Accession XM\_058994). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199796. LOC200035 (Accession XM\_055305) is another VGAM1956 host target gene. LOC200035 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC200035, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200035 BINDING SITE, designated SEQ ID:36263, to

the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66174] Another function of VGAM1956 is therefore inhibition of LOC200035 (Accession XM\_055305). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200035. LOC201707 (Accession XM\_114369) is another VGAM1956 host target gene. LOC201707 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201707, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201707 BINDING SITE, designated SEQ ID:42902, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66175] Another function of VGAM1956 is therefore inhibition of LOC201707 (Accession XM\_114369). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201707. LOC202020 (Accession XM\_114419) is another VGAM1956 host target gene. LOC202020 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC202020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202020 BINDING SITE, designated SEQ ID:42953, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66176] Another function of VGAM1956 is therefore inhibition of LOC202020 (Accession XM\_114419). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202020. LOC202934 (Accession XM\_117486) is another VGAM1956 host target gene. LOC202934 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202934 BINDING SITE, designated SEQ ID:43464, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66177] Another function of VGAM1956 is therefore inhibition of LOC202934 (Accession XM\_117486). Accordingly, utilities

of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202934. LOC205085 (Accession XM\_119810) is another VGAM1956 host target gene. LOC205085 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC205085, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205085 BINDING SITE, designated SEQ ID:43599, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66178] Another function of VGAM1956 is therefore inhibition of LOC205085 (Accession XM\_119810). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205085. LOC219649 (Accession XM\_167562) is another VGAM1956 host target gene. LOC219649 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC219649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC219649 BINDING SITE, designated SEQ ID:44667, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66179] Another function of VGAM1956 is therefore inhibition of LOC219649 (Accession XM\_167562). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219649. LOC220020 (Accession XM\_167821) is another VGAM1956 host target gene. LOC220020 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220020 BINDING SITE, designated SEQ ID:44866, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66180] Another function of VGAM1956 is therefore inhibition of LOC220020 (Accession XM\_167821). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220020. LOC220906 (Accession XM\_166133) is another VGAM1956 host target gene. LOC220906 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220906 BINDING SITE, designated SEQ ID:43927, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66181] Another function of VGAM1956 is therefore inhibition of LOC220906 (Accession XM\_166133). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220906. LOC253758 (Accession XM\_173067) is another VGAM1956 host target gene. LOC253758 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253758, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253758 BINDING SITE, designated SEQ ID:46319, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66182] Another function of VGAM1956 is therefore inhibition of

LOC253758 (Accession XM\_173067). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253758. LOC253782 (Accession XM\_171023) is another VGAM1956 host target gene. LOC253782 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253782 BINDING SITE, designated SEQ ID:45801, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66183] Another function of VGAM1956 is therefore inhibition of LOC253782 (Accession XM\_171023). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253782. LOC254170 (Accession XM\_170746) is another VGAM1956 host target gene. LOC254170 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-



illustrates the complementarity of the nucleotide sequences of LOC254170 BINDING SITE, designated SEQ ID:45504, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66184] Another function of VGAM1956 is therefore inhibition of LOC254170 (Accession XM\_170746). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254170. LOC255465 (Accession XM\_173206) is another VGAM1956 host target gene. LOC255465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255465 BINDING SITE, designated SEQ ID:46456, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66185] Another function of VGAM1956 is therefore inhibition of LOC255465 (Accession XM\_173206). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255465. LOC255520 (Accession XM\_171073) is an-

other VGAM1956 host target gene. LOC255520 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC255520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255520 BINDING SITE, designated SEQ ID:45879, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66186] Another function of VGAM1956 is therefore inhibition of LOC255520 (Accession XM\_171073). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255520. LOC54103 (Accession XM\_168508) is another VGAM1956 host target gene. LOC54103 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC54103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC54103 BINDING SITE, designated SEQ ID:45207, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66187] Another function of VGAM1956 is therefore inhibition of LOC54103 (Accession XM\_168508). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC54103. LOC58525 (Accession XM\_086045) is another VGAM1956 host target gene. LOC58525 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC58525, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58525 BINDING SITE, designated SEQ ID:38459, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66188] Another function of VGAM1956 is therefore inhibition of LOC58525 (Accession XM\_086045). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58525. LOC84570 (Accession NM\_032518) is another VGAM1956 host target gene. LOC84570 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC84570, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC84570 BINDING SITE, designated SEQ ID:26267, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66189] Another function of VGAM1956 is therefore inhibition of LOC84570 (Accession NM\_032518). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC84570. LOC89985 (Accession XM\_027892) is another VGAM1956 host target gene. LOC89985 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89985, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89985 BINDING SITE, designated SEQ ID:30584, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66190] Another function of VGAM1956 is therefore inhibition of LOC89985 (Accession XM\_027892). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC89985. LOC90170 (Accession XM\_029589) is another VGAM1956 host target gene. LOC90170 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90170 BINDING SITE, designated SEQ ID:30911, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66191] Another function of VGAM1956 is therefore inhibition of LOC90170 (Accession XM\_029589). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90170. LOC90408 (Accession XM\_031517) is another VGAM1956 host target gene. LOC90408 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90408 BINDING SITE, designated SEQ ID:31398, to the nucleotide sequence of VGAM1956 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4667.

[66192] Another function of VGAM1956 is therefore inhibition of LOC90408 (Accession XM\_031517). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90408. LOC90509 (Accession XM\_032209) is another VGAM1956 host target gene. LOC90509 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90509 BINDING SITE, designated SEQ ID:31612, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66193] Another function of VGAM1956 is therefore inhibition of LOC90509 (Accession XM\_032209). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90509. LOC90624 (Accession XM\_033003) is another VGAM1956 host target gene. LOC90624 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90624, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90624 BINDING SITE, designated SEQ ID:31816, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66194] Another function of VGAM1956 is therefore inhibition of LOC90624 (Accession XM\_033003). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90624. LOC90625 (Accession XM\_033004) is another VGAM1956 host target gene. LOC90625 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90625, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90625 BINDING SITE, designated SEQ ID:31819, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66195] Another function of VGAM1956 is therefore inhibition of LOC90625 (Accession XM\_033004). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC90625. LOC90785 (Accession XM\_034110) is another VGAM1956 host target gene. LOC90785 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90785, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90785 BINDING SITE, designated SEQ ID:32008, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66196] Another function of VGAM1956 is therefore inhibition of LOC90785 (Accession XM\_034110). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90785. LOC91818 (Accession XM\_040878) is another VGAM1956 host target gene. LOC91818 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91818, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91818 BINDING SITE, designated SEQ ID:33405, to the



nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66197] Another function of VGAM1956 is therefore inhibition of LOC91818 (Accession XM\_040878). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91818. LOC91948 (Accession XM\_041723) is another VGAM1956 host target gene. LOC91948 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91948, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91948 BINDING SITE, designated SEQ ID:33575, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66198] Another function of VGAM1956 is therefore inhibition of LOC91948 (Accession XM\_041723). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91948. LOC92661 (Accession XM\_046465) is another VGAM1956 host target gene. LOC92661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC92661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92661 BINDING SITE, designated SEQ ID:34727, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66199] Another function of VGAM1956 is therefore inhibition of LOC92661 (Accession XM\_046465). Accordingly, utilities of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92661. LOC93626 (Accession XM\_052635) is another VGAM1956 host target gene. LOC93626 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93626, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93626 BINDING SITE, designated SEQ ID:36044, to the nucleotide sequence of VGAM1956 RNA, herein designated VGAM RNA, also designated SEQ ID:4667.

[66200] Another function of VGAM1956 is therefore inhibition of LOC93626 (Accession XM\_052635). Accordingly, utilities

of VGAM1956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93626. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1957 (VGAM1957) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[66201] VGAM1957 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1957 was detected is described hereinabove with reference to Figs. 1–8.

[66202] VGAM1957 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1957 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[66203] VGAM1957 gene encodes a VGAM1957 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1957 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1957 precursor RNA is designated SEQ ID:1943, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1943 is located at position 5479 relative to the genome of Macaca Mulatta Rhadinovirus.

[66204] VGAM1957 precursor RNA folds onto itself, forming VGAM1957 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[66205] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1957 folded precursor RNA into VGAM1957 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1957 RNA is designated SEQ ID:4668, and

is provided hereinbelow with reference to the sequence listing part.

[66206] VGAM1957 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1957 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1957 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[66207] VGAM1957 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1957 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1957 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1957 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1957 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[66208] The complementary binding of VGAM1957 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1957 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1957 host target RNA into VGAM1957 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[66209] It is appreciated that VGAM1957 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1957 host target genes. The mRNA of each one of this plurality of VGAM1957 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1957 RNA, herein designated VGAM RNA, and which when bound by VGAM1957 RNA causes inhibition of translation of respective one or more VGAM1957 host target proteins.

[66210] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1957 gene, herein designated VGAM GENE, on one or more VGAM1957 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[66211] It is yet further appreciated that a function of VGAM1957 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1957 correlate with, and may be deduced from, the identity of the host target genes which VGAM1957 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[66212] Nucleotide sequences of the VGAM1957 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1957 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1957 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1957 are further described hereinbelow with reference to Table 1.

[66213] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1957 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1957 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[66214] As mentioned hereinabove with reference to Fig. 1, a



function of VGAM1957 gene, herein designated VGAM is inhibition of expression of VGAM1957 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1957 correlate with, and may be deduced from, the identity of the target genes which VGAM1957 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[66215] ATP-binding Cassette, Sub-family B (MDR/TAP), Member 4 (ABCB4, Accession NM\_000443) is a VGAM1957 host target gene. ABCB4 BINDING SITE1 and ABCB4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABCB4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCB4 BINDING SITE1 and ABCB4 BINDING SITE2, designated SEQ ID:6031 and SEQ ID:20836 respectively, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66216] A function of VGAM1957 is therefore inhibition of ATP-binding Cassette, Sub-family B (MDR/TAP), Member 4 (ABCB4, Accession NM\_000443). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ABCB4. Adenylate Kinase 1 (AK1, Accession NM\_000476) is another VGAM1957 host target gene. AK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AK1 BINDING SITE, designated SEQ ID:6088, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66217] Another function of VGAM1957 is therefore inhibition of Adenylate Kinase 1 (AK1, Accession NM\_000476). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AK1. Beta-site APP-cleaving Enzyme (BACE, Accession NM\_012104) is another VGAM1957 host target gene. BACE BINDING SITE1 and BACE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BACE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BACE BINDING SITE1

and BACE BINDING SITE2, designated SEQ ID:14417 and SEQ ID:29085 respectively, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66218] Another function of VGAM1957 is therefore inhibition of Beta-site APP-cleaving Enzyme (BACE, Accession NM\_012104), a gene which is responsible for the proteolytic processing of the amyloid precursor protein. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BACE. The function of BACE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173. BCLG (Accession NM\_030766) is another VGAM1957 host target gene. BCLG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCLG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCLG BINDING SITE, designated SEQ ID:25051, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66219] Another function of VGAM1957 is therefore inhibition of BCLG (Accession NM\_030766). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCLG. BN51 (BHK21) Temperature Sensitivity Complementing (BN51T, Accession XM\_113557) is another VGAM1957 host target gene. BN51T BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BN51T, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BN51T BINDING SITE, designated SEQ ID:42285, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66220] Another function of VGAM1957 is therefore inhibition of BN51 (BHK21) Temperature Sensitivity Complementing (BN51T, Accession XM\_113557), a gene which complements a temperature-sensitive cell cycle mutation in BHK cells. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BN51T. The function of BN51T and its association with various diseases and clinical condi-

tions, has been established by previous studies, as described hereinabove with reference to VGAM592. Cyclin-dependent Kinase Inhibitor 1B (p27, Kip1) (CDKN1B, Accession NM\_004064) is another VGAM1957 host target gene. CDKN1B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDKN1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN1B BINDING SITE, designated SEQ ID:10273, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66221] Another function of VGAM1957 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 1B (p27, Kip1) (CDKN1B, Accession NM\_004064), a gene which is involved in g1 arrest and may mediate tgf beta-induced g1 arrest. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN1B. The function of CDKN1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM592. Casein

Kinase 1, Epsilon (CSNK1E, Accession XM\_170996) is another VGAM1957 host target gene. CSNK1E BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CSNK1E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSNK1E BINDING SITE, designated SEQ ID:45773, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66222] Another function of VGAM1957 is therefore inhibition of Casein Kinase 1, Epsilon (CSNK1E, Accession XM\_170996), a gene which can phosphorylate a large number of proteins. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSNK1E. The function of CSNK1E has been established by previous studies. Casein kinase I is a member of the serine/threonine protein kinases. In fact, it consists of a family of related enzymes that are monomeric and widely distributed. Fish et al. (1995) cloned a member of the family, which they designated CKI-epsilon, from a human placenta cDNA library. The reading frame predicts a basic protein of 416 amino acids

(43.7 kD) which is most closely related to CKI-delta (OMIM Ref. No. 600864). The authors mapped the gene to 22q12-q13 by fluorescence in situ hybridization. Northern blots showed a major 2.9-kb transcript in all human cell lines examined. Recombinantly expressed enzyme was shown to phosphorylate known CKI substrates and was inhibited by CKI-7, a CKI-specific inhibitor. The human gene was able to rescue yeast with a slow-growth phenotype caused by deletion of HRR25, a yeast CKI locus. Kloss et al. (1998) cloned the double-time (dbt) gene in *Drosophila* and noted that it is most closely related to human casein kinase I-epsilon. *Drosophila* dbtS and dbtL mutations, which alter period length of *Drosophila* circadian rhythms, produce single amino acid changes in conserved regions of the predicted kinase. The dbt mRNA appears to be expressed in the same cell types as are *Drosophila* 'per' (OMIM Ref. No. 602260) and 'tim.' Dbt is capable of binding to per in vitro and in *Drosophila* cells, suggesting that a physical association of per and dbt regulates per phosphorylation and accumulation in vivo

[66223] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [66224] Fish, K. J.; Cegielska, A.; Getman, M. E.; Landes, G. M.; Virshup, D. M. : Isolation and characterization of human casein kinase I-epsilon (CKI), a novel member of the CKI gene family. J. Biol. Chem. 270: 14875-14883, 1995. ; and
- [66225] Kloss, B.; Price, J. L.; Saez, L.; Blau, J.; Rothenfluh, A.; Wesley, C. S.; Young, M. W. : The Drosophila clock gene double-time encodes a protein closely-related to human casein kinase.
- [66226] Further studies establishing the function and utilities of CSNK1E are found in John Hopkins OMIM database record ID 600863, and in cited publications numbered 7013-7015 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM\_166434) is another VGAM1957 host target gene. DAAM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAAM2 BINDING SITE, designated SEQ ID:44331, to the nucleotide sequence of



VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66227] Another function of VGAM1957 is therefore inhibition of Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM\_166434), a gene which controls cell polarity and movement during development. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAAM2. The function of DAAM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Deoxycytidine Kinase (DCK, Accession NM\_000788) is another VGAM1957 host target gene. DCK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCK BINDING SITE, designated SEQ ID:6441, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66228] Another function of VGAM1957 is therefore inhibition of Deoxycytidine Kinase (DCK, Accession NM\_000788), a

gene which mediates the phosphorylation of several deoxyribonucleosides and their analogs. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCK. The function of DCK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM538. Death Effector Domain Containing (DEDD, Accession NM\_032998) is another VGAM1957 host target gene. DEDD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DEDD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEDD BINDING SITE, designated SEQ ID:26881, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66229] Another function of VGAM1957 is therefore inhibition of Death Effector Domain Containing (DEDD, Accession NM\_032998), a gene which intervenes in apoptosis. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with DEDD. The function of DEDD and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1189.DNA

(cytosine-5-)-methyltransferase 2 (DNMT2, Accession NM\_004412) is another VGAM1957 host target gene.

DNMT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNMT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of DNMT2 BINDING SITE, designated SEQ

ID:10671, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ

ID:4668.

[66230] Another function of VGAM1957 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 2 (DNMT2, Accession NM\_004412), a gene which may mark specific sequences in the genome . Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT2. The function of DNMT2 and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM177. Down Syndrome Critical Region Gene 4 (DSCR4, Accession NM\_005867) is another VGAM1957 host target gene. DSCR4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DSCR4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSCR4 BINDING SITE, designated SEQ ID:12488, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66231] Another function of VGAM1957 is therefore inhibition of Down Syndrome Critical Region Gene 4 (DSCR4, Accession NM\_005867). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSCR4. G Protein-coupled Receptor 81 (GPR81, Accession NM\_032554) is another VGAM1957 host target gene. GPR81 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR81, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR81 BINDING SITE, designated SEQ ID:12489, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

tarity of the nucleotide sequences of GPR81 BINDING SITE, designated SEQ ID:26279, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66232] Another function of VGAM1957 is therefore inhibition of G Protein-coupled Receptor 81 (GPR81, Accession NM\_032554). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR81. Glutathione S-transferase M5 (GSTM5, Accession NM\_000851) is another VGAM1957 host target gene. GSTM5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GSTM5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GSTM5 BINDING SITE, designated SEQ ID:6519, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66233] Another function of VGAM1957 is therefore inhibition of Glutathione S-transferase M5 (GSTM5, Accession NM\_000851), a gene which conjugates reduced glutathione to a wide number of exogenous and endogenous

hydrophobic electrophiles. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GSTM5. The function of GSTM5 has been established by previous studies. The glutathione S-transferases (GSTs) are dimeric enzymes that metabolize a broad range of xenobiotics and carcinogens. They are encoded by several multigene families. See GSTM1 (OMIM Ref. No. 138350) for additional background. By screening a human frontal cortex cDNA library with a rat cDNA that cross-hybridized with other rodent and human mu class GST cDNAs, Takahashi et al. (1993) isolated a cDNA encoding GSTM5. Northern blot analysis revealed that GSTM5 is expressed primarily in brain and lung and to a lesser extent in heart. The GSTM5 gene encodes a predicted 217-amino acid protein. By Western blot analysis using antibodies against the unique C-terminal region of GSTM5, Takahashi et al. (1993) detected GSTM5 in brain and testis but not liver.

[66234] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66235] Pearson, W. R.; Vorachek, W. R.; Xu, S.; Berger, R.; Hart, I.; Vannais, D.; Patterson, D. : Identification of class-mu glu-

tathione transferase genes GSTM1–GSTM5 on human chromosome 1p13. Am. J. Hum. Genet. 53: 220–233, 1993. ; and

[66236] Takahashi, Y.; Campbell, E. A.; Hirata, Y.; Takayama, T.; Listowsky, I. : A basis for differentiating among the multiple human mu–glutathione S–transferases and molecular cloning of bra.

[66237] Further studies establishing the function and utilities of GSTM5 are found in John Hopkins OMIM database record ID 138385, and in cited publications numbered 3730 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Huntingtin (Huntington disease) (HD, Accession NM\_002111) is another VGAM1957 host target gene. HD BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HD BINDING SITE, designated SEQ ID:7896, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66238] Another function of VGAM1957 is therefore inhibition of

Huntingtin (Huntington disease) (HD, Accession NM\_002111). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HD. Homeo Box B9 (HOXB9, Accession NM\_024017) is another VGAM1957 host target gene. HOXB9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HOXB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXB9 BINDING SITE, designated SEQ ID:23447, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66239] Another function of VGAM1957 is therefore inhibition of Homeo Box B9 (HOXB9, Accession NM\_024017). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXB9. HTRA3 (Accession XM\_114416) is another VGAM1957 host target gene. HTRA3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HTRA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTRA3 BINDING SITE, designated SEQ ID:42938, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66240] Another function of VGAM1957 is therefore inhibition of HTRA3 (Accession XM\_114416). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTRA3. Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM\_012275) is another VGAM1957 host target gene. IL1F5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1F5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1F5 BINDING SITE, designated SEQ ID:14604, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66241] Another function of VGAM1957 is therefore inhibition of Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM\_012275), a gene which is a novel interleukin-1 receptor antagonist gene. Accordingly, utilities of VGAM1957

include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F5. The function of IL1F5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM263. Potassium Voltage-gated Channel, KQT-like Subfamily, Member 3 (KCNQ3, Accession NM\_004519) is another VGAM1957 host target gene. KCNQ3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNQ3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNQ3 BINDING SITE, designated SEQ ID:10847, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66242] Another function of VGAM1957 is therefore inhibition of Potassium Voltage-gated Channel, KQT-like Subfamily, Member 3 (KCNQ3, Accession NM\_004519), a gene which probably important in the regulation of neuronal excitability. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNQ3. The function of

KCNQ3 has been established by previous studies. The KQT-like family is a family of voltage-gated potassium channels. The first human gene belonging to this family to be identified was that responsible for chromosome-11 long QT syndrome and the Jervell and Lange-Nielsen cardioauditory syndrome (KCNQ1; 192500). The second to be identified (KCNQ2; 602235) was the gene mutated in the chromosome-20 form of benign neonatal epilepsy (EBN1; 121200). To identify new members of that family, possibly implicated in other forms of idiopathic generalized epilepsy, Charlier et al. (1998) conducted a tBLASTx search with the KCNQ2 full-length cDNA against the expressed sequence tag (EST) database. In this way they identified a new gene, designated KCNQ3. They mapped the gene to chromosome 8 by analysis of a somatic cell hybrid panel and refined the assignment by analysis of radiation hybrids, which showed tight linkage of KCNQ3 to markers previously mapped to 8q24. The KCNQ3 gene was localized to the interval defined by markers previously linked to a family with chromosome-8 benign neonatal epilepsy (EBN2; 121201). Charlier et al. (1998) then sought mutations in the KCNQ3 gene in a member of a phenotypically well-characterized 3-generation Mexican-

American family affected with BFNC2 reported by Ryan et al. (1991). They identified a single heterozygous missense mutation, glycine (GGC) to valine (GTC), in position 263 of the highly conserved pore region. The same glycine had been found to be mutated in KCNQ1 (gly177arg) in a patient with long QT syndrome (192500.0001). Defects in the KCNQ genes cause human disorders associated with altered regulation of excitability. KCNQ1 is expressed in the heart and inner ear; KCNQ2 and KCNQ3 are expressed in the brain Cooper et al. (2000) provided information regarding the in vivo distribution and biochemical characteristics of human brain KCNQ2 and KCNQ3, the 2 channel subunits that form M-channels when expressed in vitro, and, when mutated, cause the dominantly inherited epileptic syndrome, benign familial neonatal convulsions. They found that the KCNQ2 and KCNQ3 proteins are colocalized in a somatodendritic pattern on pyramidal and polymorphic neurons in the human cortex and hippocampus. Immunoreactivity for KCNQ2, but not KCNQ3, is also prominent in some terminal fields, suggesting a presynaptic role for a distinct subgroup of M-channels in the regulation of action potential propagation and neurotransmitter release. KCNQ2 and KCNQ3 could be coim-

munoprecipitated from brain lysates. Further, both proteins were coassociated with tubulin (see OMIM Ref. No. 602529) and protein kinase A (see OMIM Ref. No. 176911) within a triton X-100-insoluble protein complex. Cooper et al. (2000) suggested that these studies provided a view of a signaling complex that may be important for cognitive function as well as epilepsy, and that analysis of this complex may shed light on the transduction pathway linking muscarinic acetylcholine receptor (see OMIM Ref. No. 118510) activation to M-channel inhibition.

[66243] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66244] Cooper, E. C.; Aldape, K. D.; Abosch, A.; Barbaro, N. M.; Berger, M. S.; Peacock, W. S.; Jan, Y. N.; Jan, L. Y. : Colocalization and coassembly of two human brain M-type potassium channel subunits that are mutated in epilepsy. Proc. Nat. Acad. Sci. 97: 4914-4919, 2000. ; and

[66245] Charlier, C.; Singh, N. A.; Ryan, S. G.; Lewis, T. B.; Reus, B. E.; Leach, R. J.; Leppert, M. : A pore mutation in a novel KQT-like potassium channel gene in an idiopathic epilepsy fami.

[66246] Further studies establishing the function and utilities of

KCNQ3 are found in John Hopkins OMIM database record ID 602232, and in cited publications numbered 4664, 628 and 6290–6291 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Potassium Voltage–gated Channel, Delayed–rectifier, Subfamily S, Member 2 (KCNS2, Accession XM\_043106) is another VGAM1957 host target gene. KCNS2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KCNS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNS2 BINDING SITE, designated SEQ ID:33898, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66247] Another function of VGAM1957 is therefore inhibition of Potassium Voltage–gated Channel, Delayed–rectifier, Subfamily S, Member 2 (KCNS2, Accession XM\_043106), a gene which mediates the voltage–dependent potassium ion permeability of excitable membranes. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNS2. The function of KCNS2 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM419. Loss of Heterozygosity, 11, Chromosomal Region 2, Gene A (LOH11CR2A, Accession NM\_014622) is another VGAM1957 host target gene. LOH11CR2A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOH11CR2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOH11CR2A BINDING SITE, designated SEQ ID:15989, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66248] Another function of VGAM1957 is therefore inhibition of Loss of Heterozygosity, 11, Chromosomal Region 2, Gene A (LOH11CR2A, Accession NM\_014622). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOH11CR2A. V-maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog F (avian) (MAFF, Accession NM\_012323) is another VGAM1957 host target gene. MAFF BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by MAFF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAFF BINDING SITE, designated SEQ ID:14702, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66249] Another function of VGAM1957 is therefore inhibition of V-maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog F (avian) (MAFF, Accession NM\_012323), a gene which Binds to the US-2 motif of the oxytocin receptor gene; has a leucine zipper structure. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAFF. The function of MAFF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1928. Mitogen-activated Protein Kinase 14 (MAPK14, Accession NM\_139012) is another VGAM1957 host target gene. MAPK14 BINDING SITE1 through MAPK14 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPK14, corresponding to HOST TARGET binding sites



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK14 BINDING SITE1 through MAPK14 BINDING SITE3, designated SEQ ID:29108, SEQ ID:7004 and SEQ ID:29115 respectively, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66250] Another function of VGAM1957 is therefore inhibition of Mitogen-activated Protein Kinase 14 (MAPK14, Accession NM\_139012), a gene which is important for cytokine production; responds to changes in extracellular osmolarity. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK14. The function of MAPK14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. MAX Protein (MAX, Accession NM\_145112) is another VGAM1957 host target gene. MAX BINDING SITE1 through MAX BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAX, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MAX BINDING SITE1 through MAX BINDING SITE4, designated SEQ ID:29717, SEQ ID:29719, SEQ ID:29722 and SEQ ID:22487 respectively, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66251] Another function of VGAM1957 is therefore inhibition of MAX Protein (MAX, Accession NM\_145112), a gene which interacts specifically with the MYC (190080) protein . Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAX. The function of MAX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1923. Procollagen C-endopeptidase Enhancer 2 (PCOLCE2, Accession NM\_013363) is another VGAM1957 host target gene. PCOLCE2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PCOLCE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCOLCE2 BINDING SITE, designated SEQ ID:15009, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66252] Another function of VGAM1957 is therefore inhibition of Procollagen C-endopeptidase Enhancer 2 (PCOLCE2, Accession NM\_013363), a gene which binds to the cooh-

terminal propeptide of type I procollagen and enhances procollagen C-proteinase activity. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCOLCE2. The function of PCOLCE2 has been established by previous studies. Xu et al. (2000) cloned PCOLCE2 from trabecular meshwork cell mRNA followed by 5-prime RACE. The deduced 415-amino acid protein contains an N-terminal signal sequence, 2 CUB domains, and an NTR domain. It also contains a putative myristoylation site, several potential phosphorylation sites, a putative glycosylation site, and an RGD site. PCOLCE2 shares about 43% sequence identity with the PCOLCE protein (OMIM Ref. No. 600270). The secreted PCOLCE2 protein is calculated to have a molecular mass of about 47 kD. Northern blot analysis detected ubiquitous expression of a 2-kb transcript, with highest expression in heart, placenta, and trabecular meshwork, and very low expression in brain. Western blot analysis revealed a 52-kD form of PCOLCE2 in human fibroblast cells. Xu et al. (2000) identified the PCOLCE2 sequence within an EST mapped to chromosome 3q21-q24. Steiglitiz and Greenspan (2001) noted identity between the PCOLCE2 sequence and the sequence of a

BAC clone mapped to 3q23. They found that PCOLCE2 lies 5.2 kb and 102.5 kb centromeric to the transient receptor potential channel-1 (TRPC1; 602343) and plastin-1 (PLS1; 602734), respectively. By radiation hybrid analysis, they mapped the mouse gene to chromosome 9.

[66253] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66254] Steiglitz, B. M.; Greenspan, D. S. : Assignment of the mouse Pcolce2 gene, which encodes procollagen C-proteinase enhancer protein 2, to chromosome 9 and localization of PCOLCE2 to human chromosome 3q23. Cytogenet. Cell Genet. 95: 244-245, 2001. ; and

[66255] Xu, H.; Acott, T. S.; Wirtz, M. K. : Identification and expression of a novel type I procollagen C-proteinase enhancer protein gene from the glaucoma candidate region on 3q21-q24. Geno.

[66256] Further studies establishing the function and utilities of PCOLCE2 are found in John Hopkins OMIM database record ID 607064, and in cited publications numbered 5133-5134 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Phosphatase, EF Hand Calcium-binding Domain 2 (PPEF2,

Accession NM\_006239) is another VGAM1957 host target gene. PPEF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPEF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPEF2 BINDING SITE, designated SEQ ID:12904, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66257] Another function of VGAM1957 is therefore inhibition of Protein Phosphatase, EF Hand Calcium-binding Domain 2 (PPEF2, Accession NM\_006239), a gene which is a homolog of *Drosophila* rdgC. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPEF2. The function of PPEF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1466. RAB3A, Member RAS Oncogene Family (RAB3A, Accession NM\_002866) is another VGAM1957 host target gene. RAB3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB3A, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB3A BINDING SITE, designated SEQ ID:8770, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66258] Another function of VGAM1957 is therefore inhibition of RAB3A, Member RAS Oncogene Family (RAB3A, Accession NM\_002866), a gene which is involved in exocytosis, by regulating a late step in synaptic vesicle fusion. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB3A. The function of RAB3A has been established by previous studies. The RAS gene superfamily is divided into 3 main branches according to protein homology. In mammals the first branch includes the classic RAS genes as well as RAL (OMIM Ref. No. 179550) and RRAS (OMIM Ref. No. 165090). The RHO genes (165370, 165380, 165390) belong to the second branch and the RAB genes to the third. The RAB genes were so named because they were first isolated from a rat brain library. Zahraoui et al. (1989) isolated cDNAs encoding RAB3A and several other human RAB proteins. See RAB5A (OMIM

Ref. No. 179512). The predicted 220–amino acid human RAB3A protein shares 99% and 78% identity with rat Rab3A and human RAB3B (OMIM Ref. No. 179510), respectively. Animal model experiments lend further support to the function of RAB3A. In brain, RAB3A is found specifically in synaptic vesicles. Geppert et al. (1997) generated Rab3A–deficient mice. They found that the size of the readily releasable pool of vesicles was normal, but that calcium–triggered fusion was altered in the absence of Rab3A such that a greater number of exocytic events occurred within a brief time after arrival of the nerve impulse. They concluded that Rab3A regulates a late step in synaptic vesicle fusion.

[66259] It is appreciated that the abovementioned animal model for RAB3A is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[66260] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66261] Zahraoui, A.; Touchot, N.; Chardin, P.; Tavitian, A. : The human rab genes encode a family of GTP–binding proteins related to yeast YPT1 and SEC4 products involved in se–



cretion. J. Biol. Chem. 264: 12394–12401, 1989. ; and

[66262] Geppert, M.; Goda, Y.; Stevens, C. F.; Sudhof, T. C. : The small GTP-binding protein Rab3A regulates a late step in synaptic vesicle fusion. Nature 387: 810–814, 1997.

[66263] Further studies establishing the function and utilities of RAB3A are found in John Hopkins OMIM database record ID 179490, and in cited publications numbered 2718–272 and 5126 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Retinoid X Receptor, Alpha (RXRA, Accession NM\_002957) is another VGAM1957 host target gene. RXRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RXRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RXRA BINDING SITE, designated SEQ ID:8871, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66264] Another function of VGAM1957 is therefore inhibition of Retinoid X Receptor, Alpha (RXRA, Accession NM\_002957), a gene which activates genes required for vitamin A metabolism, binds 9-cis retinoic acid. Accordingly, utili-

ties of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RXRA. The function of RXRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM349. TEM6 (Accession NM\_022748) is another VGAM1957 host target gene. TEM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM6 BINDING SITE, designated SEQ ID:22960, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66265] Another function of VGAM1957 is therefore inhibition of TEM6 (Accession NM\_022748), a gene which displays elevated expression during tumor angiogenesis. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM6. The function of TEM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM175.Tumor Protein D52-like 2 (TPD52L2, Accession NM\_003288) is another VGAM1957 host target gene. TPD52L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TPD52L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPD52L2 BINDING SITE, designated SEQ ID:9298, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66266] Another function of VGAM1957 is therefore inhibition of Tumor Protein D52-like 2 (TPD52L2, Accession NM\_003288). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPD52L2. Tripartite Motif-containing 34 (TRIM34, Accession NM\_021616) is another VGAM1957 host target gene. TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRIM34, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2, designated SEQ ID:22251 and SEQ ID:28175 respectively, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66267] Another function of VGAM1957 is therefore inhibition of Tripartite Motif-containing 34 (TRIM34, Accession NM\_021616). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM34. Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM\_014919) is another VGAM1957 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:17177, SEQ ID:28458 and SEQ ID:9448 respectively, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66268] Another function of VGAM1957 is therefore inhibition of

Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM\_014919), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577) is another VGAM1957 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31076, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66269] Another function of VGAM1957 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with ATP9A. Bladder Cancer Associated Protein (BLCAP, Accession NM\_006698) is another VGAM1957 host target gene. BLCAP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BLCAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLCAP BINDING SITE, designated SEQ ID:13519, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66270] Another function of VGAM1957 is therefore inhibition of Bladder Cancer Associated Protein (BLCAP, Accession NM\_006698). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLCAP. Bromodomain Containing 4 (BRD4, Accession NM\_058243) is another VGAM1957 host target gene. BRD4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BRD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRD4 BINDING SITE,

designated SEQ ID:27774, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66271] Another function of VGAM1957 is therefore inhibition of Bromodomain Containing 4 (BRD4, Accession NM\_058243). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRD4. Catenin, Beta Interacting Protein 1 (CTNNBIP1, Accession NM\_020248) is another VGAM1957 host target gene. CTNNBIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTNNBIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTNNBIP1 BINDING SITE, designated SEQ ID:21544, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66272] Another function of VGAM1957 is therefore inhibition of Catenin, Beta Interacting Protein 1 (CTNNBIP1, Accession NM\_020248). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTNNBIP1. DKFZP566K1924

(Accession XM\_057469) is another VGAM1957 host target gene. DKFZP566K1924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566K1924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566K1924 BINDING SITE, designated SEQ ID:36517, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66273] Another function of VGAM1957 is therefore inhibition of DKFZP566K1924 (Accession XM\_057469). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566K1924. DKFZP667O116 (Accession XM\_168586) is another VGAM1957 host target gene. DKFZP667O116 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP667O116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP667O116 BINDING SITE, designated SEQ ID:45265, to the nucleotide sequence of



VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66274] Another function of VGAM1957 is therefore inhibition of DKFZP667O116 (Accession XM\_168586). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP667O116. FBX30 (Accession NM\_033182) is another VGAM1957 host target gene. FBX30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBX30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBX30 BINDING SITE, designated SEQ ID:27041, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66275] Another function of VGAM1957 is therefore inhibition of FBX30 (Accession NM\_033182). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBX30. FLJ10079 (Accession XM\_012540) is another VGAM1957 host target gene. FLJ10079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ10079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10079 BINDING SITE, designated SEQ ID:30216, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66276] Another function of VGAM1957 is therefore inhibition of FLJ10079 (Accession XM\_012540). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10079. FLJ11164 (Accession NM\_018346) is another VGAM1957 host target gene. FLJ11164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11164 BINDING SITE, designated SEQ ID:20357, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66277] Another function of VGAM1957 is therefore inhibition of FLJ11164 (Accession NM\_018346). Accordingly, utilities of

VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11164. FLJ11506 (Accession NM\_024666) is another VGAM1957 host target gene. FLJ11506 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11506 BINDING SITE, designated SEQ ID:23969, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66278] Another function of VGAM1957 is therefore inhibition of FLJ11506 (Accession NM\_024666). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11506. FLJ11715 (Accession NM\_024564) is another VGAM1957 host target gene. FLJ11715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11715

BINDING SITE, designated SEQ ID:23788, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66279] Another function of VGAM1957 is therefore inhibition of FLJ11715 (Accession NM\_024564). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11715. FLJ12783 (Accession NM\_031426) is another VGAM1957 host target gene. FLJ12783 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12783, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12783 BINDING SITE, designated SEQ ID:25419, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66280] Another function of VGAM1957 is therefore inhibition of FLJ12783 (Accession NM\_031426). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12783. FLJ14146 (Accession NM\_024709) is another VGAM1957 host target gene. FLJ14146 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14146 BINDING SITE, designated SEQ ID:24030, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66281] Another function of VGAM1957 is therefore inhibition of FLJ14146 (Accession NM\_024709). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14146. FLJ20034 (Accession NM\_017630) is another VGAM1957 host target gene. FLJ20034 BINDING SITE1 and FLJ20034 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ20034, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20034 BINDING SITE1 and FLJ20034 BINDING SITE2, designated SEQ ID:19135 and SEQ ID:19136 respectively, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4668.

[66282] Another function of VGAM1957 is therefore inhibition of FLJ20034 (Accession NM\_017630). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20034. FLJ20312 (Accession NM\_017761) is another VGAM1957 host target gene. FLJ20312 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20312 BINDING SITE, designated SEQ ID:19374, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66283] Another function of VGAM1957 is therefore inhibition of FLJ20312 (Accession NM\_017761). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20312. FLJ20378 (Accession NM\_017795) is another VGAM1957 host target gene. FLJ20378 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20378, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20378 BINDING SITE, designated SEQ ID:19437, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66284] Another function of VGAM1957 is therefore inhibition of FLJ20378 (Accession NM\_017795). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20378. FLJ20400 (Accession XM\_039306) is another VGAM1957 host target gene. FLJ20400 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20400, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20400 BINDING SITE, designated SEQ ID:33046, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66285] Another function of VGAM1957 is therefore inhibition of FLJ20400 (Accession XM\_039306). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20400. FLJ20574 (Accession NM\_017886) is another VGAM1957 host target gene. FLJ20574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20574 BINDING SITE, designated SEQ ID:19555, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66286] Another function of VGAM1957 is therefore inhibition of FLJ20574 (Accession NM\_017886). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20574. FLJ22833 (Accession NM\_022837) is another VGAM1957 host target gene. FLJ22833 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22833, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22833 BINDING SITE, designated SEQ ID:23122, to the nucleotide



sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66287] Another function of VGAM1957 is therefore inhibition of FLJ22833 (Accession NM\_022837). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22833. FLJ23277 (Accession NM\_032236) is another VGAM1957 host target gene. FLJ23277 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23277 BINDING SITE, designated SEQ ID:25955, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66288] Another function of VGAM1957 is therefore inhibition of FLJ23277 (Accession NM\_032236). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23277. Glucocorticoid Modulatory Element Binding Protein 2 (GMEB2, Accession NM\_012384) is another VGAM1957 host target gene. GMEB2 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GMEB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GMEB2 BINDING SITE, designated SEQ ID:14739, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66289] Another function of VGAM1957 is therefore inhibition of Glucocorticoid Modulatory Element Binding Protein 2 (GMEB2, Accession NM\_012384). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMEB2. G Protein Pathway Suppressor 2 (GPS2, Accession NM\_004489) is another VGAM1957 host target gene. GPS2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPS2 BINDING SITE, designated SEQ ID:10827, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66290] Another function of VGAM1957 is therefore inhibition of G Protein Pathway Suppressor 2 (GPS2, Accession NM\_004489). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPS2. HSGP25L2G (Accession XM\_030771) is another VGAM1957 host target gene. HSGP25L2G BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSGP25L2G, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSGP25L2G BINDING SITE, designated SEQ ID:31135, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66291] Another function of VGAM1957 is therefore inhibition of HSGP25L2G (Accession XM\_030771). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSGP25L2G. KIAA0082 (Accession XM\_166400) is another VGAM1957 host target gene. KIAA0082 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0082, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0082 BINDING SITE, designated SEQ ID:44262, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66292] Another function of VGAM1957 is therefore inhibition of KIAA0082 (Accession XM\_166400). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0082. KIAA0092 (Accession NM\_014679) is another VGAM1957 host target gene. KIAA0092 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0092 BINDING SITE, designated SEQ ID:16155, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66293] Another function of VGAM1957 is therefore inhibition of KIAA0092 (Accession NM\_014679). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0092. KIAA0232 (Accession XM\_052627) is another VGAM1957 host target gene. KIAA0232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0232 BINDING SITE, designated SEQ ID:36037, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66294] Another function of VGAM1957 is therefore inhibition of KIAA0232 (Accession XM\_052627). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0232. KIAA0275 (Accession NM\_014767) is another VGAM1957 host target gene. KIAA0275 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0275 BINDING SITE, designated SEQ ID:16554, to the

nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66295] Another function of VGAM1957 is therefore inhibition of KIAA0275 (Accession NM\_014767). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0275. KIAA0321 (Accession XM\_031077) is another VGAM1957 host target gene. KIAA0321 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0321, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0321 BINDING SITE, designated SEQ ID:31270, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66296] Another function of VGAM1957 is therefore inhibition of KIAA0321 (Accession XM\_031077). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0321. KIAA0418 (Accession NM\_014631) is another VGAM1957 host target gene. KIAA0418 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0418 BINDING SITE, designated SEQ ID:15995, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66297] Another function of VGAM1957 is therefore inhibition of KIAA0418 (Accession NM\_014631). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0418. KIAA0427 (Accession NM\_014772) is another VGAM1957 host target gene. KIAA0427 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0427 BINDING SITE, designated SEQ ID:16580, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66298] Another function of VGAM1957 is therefore inhibition of KIAA0427 (Accession NM\_014772). Accordingly, utilities

of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0427. KIAA0478 (Accession NM\_014870) is another VGAM1957 host target gene. KIAA0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0478 BINDING SITE, designated SEQ ID:16983, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66299] Another function of VGAM1957 is therefore inhibition of KIAA0478 (Accession NM\_014870). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0478. KIAA0522 (Accession XM\_050404) is another VGAM1957 host target gene. KIAA0522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of



KIAA0522 BINDING SITE, designated SEQ ID:35625, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66300] Another function of VGAM1957 is therefore inhibition of KIAA0522 (Accession XM\_050404). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0522. KIAA0537 (Accession NM\_014840) is another VGAM1957 host target gene. KIAA0537 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0537, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0537 BINDING SITE, designated SEQ ID:16862, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66301] Another function of VGAM1957 is therefore inhibition of KIAA0537 (Accession NM\_014840). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0537. KIAA0652 (Accession NM\_014741) is another VGAM1957 host target gene. KIAA0652 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0652, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0652 BINDING SITE, designated SEQ ID:16406, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66302] Another function of VGAM1957 is therefore inhibition of KIAA0652 (Accession NM\_014741). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0652. KIAA1274 (Accession XM\_166125) is another VGAM1957 host target gene. KIAA1274 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1274 BINDING SITE, designated SEQ ID:43913, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66303] Another function of VGAM1957 is therefore inhibition of

KIAA1274 (Accession XM\_166125). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1274. KIAA1297 (Accession XM\_051005) is another VGAM1957 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35707, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66304] Another function of VGAM1957 is therefore inhibition of KIAA1297 (Accession XM\_051005). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. KIAA1522 (Accession XM\_036299) is another VGAM1957 host target gene. KIAA1522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1522 BINDING SITE, designated SEQ ID:32419, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66305] Another function of VGAM1957 is therefore inhibition of KIAA1522 (Accession XM\_036299). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1522. KIAA1560 (Accession XM\_034422) is another VGAM1957 host target gene. KIAA1560 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1560, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1560 BINDING SITE, designated SEQ ID:32104, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66306] Another function of VGAM1957 is therefore inhibition of KIAA1560 (Accession XM\_034422). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1560. KIAA1580 (Accession XM\_045271) is another

VGAM1957 host target gene. KIAA1580 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1580 BINDING SITE, designated SEQ ID:34408, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66307] Another function of VGAM1957 is therefore inhibition of KIAA1580 (Accession XM\_045271). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1580. KIAA1649 (Accession XM\_040095) is another VGAM1957 host target gene. KIAA1649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1649 BINDING SITE, designated SEQ ID:33258, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66308] Another function of VGAM1957 is therefore inhibition of KIAA1649 (Accession XM\_040095). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1649. KIAA1691 (Accession XM\_166523) is another VGAM1957 host target gene. KIAA1691 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1691, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1691 BINDING SITE, designated SEQ ID:44462, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66309] Another function of VGAM1957 is therefore inhibition of KIAA1691 (Accession XM\_166523). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1691. KIAA1826 (Accession XM\_040784) is another VGAM1957 host target gene. KIAA1826 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1826, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1826 BINDING SITE, designated SEQ ID:33377, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66310] Another function of VGAM1957 is therefore inhibition of KIAA1826 (Accession XM\_040784). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1826. KIAA1831 (Accession XM\_033366) is another VGAM1957 host target gene. KIAA1831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1831 BINDING SITE, designated SEQ ID:31906, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66311] Another function of VGAM1957 is therefore inhibition of KIAA1831 (Accession XM\_033366). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1831. MGC3248 (Accession NM\_032486) is another VGAM1957 host target gene. MGC3248 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3248 BINDING SITE, designated SEQ ID:26240, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66312] Another function of VGAM1957 is therefore inhibition of MGC3248 (Accession NM\_032486). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3248. MGC4549 (Accession NM\_032377) is another VGAM1957 host target gene. MGC4549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4549 BINDING SITE, designated SEQ ID:26172, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM



RNA, also designated SEQ ID:4668.

[66313] Another function of VGAM1957 is therefore inhibition of MGC4549 (Accession NM\_032377). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4549. MGC4655 (Accession NM\_033309) is another VGAM1957 host target gene. MGC4655 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4655 BINDING SITE, designated SEQ ID:27146, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66314] Another function of VGAM1957 is therefore inhibition of MGC4655 (Accession NM\_033309). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4655. N4BP3 (Accession XM\_038920) is another VGAM1957 host target gene. N4BP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by N4BP3, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP3 BINDING SITE, designated SEQ ID:32937, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66315] Another function of VGAM1957 is therefore inhibition of N4BP3 (Accession XM\_038920). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP3. poly(A) Polymerase Gamma (PAPOLG, Accession NM\_022894) is another VGAM1957 host target gene. PAPOLG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PAPOLG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAPOLG BINDING SITE, designated SEQ ID:23154, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66316] Another function of VGAM1957 is therefore inhibition of poly(A) Polymerase Gamma (PAPOLG, Accession

NM\_022894). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAPOLG. PR Domain Containing 10 (PRDM10, Accession NM\_020228) is another VGAM1957 host target gene. PRDM10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRDM10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM10 BINDING SITE, designated SEQ ID:21497, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66317] Another function of VGAM1957 is therefore inhibition of PR Domain Containing 10 (PRDM10, Accession NM\_020228). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM10. PRTD-NY3 (Accession NM\_030924) is another VGAM1957 host target gene. PRTD-NY3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRTD-NY3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRTD-NY3 BINDING SITE, designated SEQ ID:25194, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66318] Another function of VGAM1957 is therefore inhibition of PRTD-NY3 (Accession NM\_030924). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRTD-NY3. RAB10, Member RAS Oncogene Family (RAB10, Accession XM\_097979) is another VGAM1957 host target gene. RAB10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB10 BINDING SITE, designated SEQ ID:41281, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66319] Another function of VGAM1957 is therefore inhibition of RAB10, Member RAS Oncogene Family (RAB10, Accession XM\_097979). Accordingly, utilities of VGAM1957 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB10. RAS Protein Activator Like 2 (RASAL2, Accession NM\_004841) is another VGAM1957 host target gene. RASAL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASAL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASAL2 BINDING SITE, designated SEQ ID:11250, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66320] Another function of VGAM1957 is therefore inhibition of RAS Protein Activator Like 2 (RASAL2, Accession NM\_004841). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASAL2. RAS Guanyl Releasing Protein 4 (RASGRP4, Accession NM\_052949) is another VGAM1957 host target gene. RASGRP4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RASGRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of RASGRP4 BINDING SITE, designated SEQ ID:27505, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66321] Another function of VGAM1957 is therefore inhibition of RAS Guanyl Releasing Protein 4 (RASGRP4, Accession NM\_052949). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASGRP4. RNA Binding Protein S1, Serine-rich Domain (RNPS1, Accession NM\_080594) is another VGAM1957 host target gene. RNPS1 BINDING SITE1 and RNPS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RNPS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNPS1 BINDING SITE1 and RNPS1 BINDING SITE2, designated SEQ ID:27902 and SEQ ID:13537 respectively, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66322] Another function of VGAM1957 is therefore inhibition of RNA Binding Protein S1, Serine-rich Domain (RNPS1, Ac-

cession NM\_080594). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNPS1. Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3E (SEMA3E, Accession NM\_012431) is another VGAM1957 host target gene. SEMA3E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA3E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA3E BINDING SITE, designated SEQ ID:14808, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66323] Another function of VGAM1957 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3E (SEMA3E, Accession NM\_012431). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA3E. Sialyltransferase 8A (alpha-N-acetylneuraminate: alpha-2,8-sialyltransferase, GD3 synthase) (SIAT8A, Accession

NM\_003034) is another VGAM1957 host target gene. SIAT8A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SIAT8A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT8A BINDING SITE, designated SEQ ID:8983, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66324] Another function of VGAM1957 is therefore inhibition of Sialyltransferase 8A (alpha-N-acetylneuraminate: alpha-2,8-sialyltransferase, GD3 synthase) (SIAT8A, Accession NM\_003034). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT8A. Serum Response Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM\_003131) is another VGAM1957 host target gene. SRF BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity



of the nucleotide sequences of SRF BINDING SITE, designated SEQ ID:9103, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66325] Another function of VGAM1957 is therefore inhibition of Serum Response Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM\_003131). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRF. Serine/threonine Kinase 38 Like (STK38L, Accession XM\_044823) is another VGAM1957 host target gene. STK38L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK38L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK38L BINDING SITE, designated SEQ ID:34286, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66326] Another function of VGAM1957 is therefore inhibition of Serine/threonine Kinase 38 Like (STK38L, Accession XM\_044823). Accordingly, utilities of VGAM1957 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with STK38L. Sulfotransferase Family, Cytosolic, 1C, Member 2 (SULT1C2, Accession NM\_006588) is another VGAM1957 host target gene. SULT1C2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SULT1C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SULT1C2 BINDING SITE, designated SEQ ID:13354, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66327] Another function of VGAM1957 is therefore inhibition of Sulfotransferase Family, Cytosolic, 1C, Member 2 (SULT1C2, Accession NM\_006588). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SULT1C2. Synaptotagmin-like 4 (granuphilin-a) (SYTL4, Accession NM\_080737) is another VGAM1957 host target gene. SYTL4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SYTL4, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYTL4 BINDING SITE, designated SEQ ID:28023, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66328] Another function of VGAM1957 is therefore inhibition of Synaptotagmin-like 4 (granuphilin-a) (SYTL4, Accession NM\_080737). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYTL4. T-box 21 (TBX21, Accession NM\_013351) is another VGAM1957 host target gene. TBX21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBX21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBX21 BINDING SITE, designated SEQ ID:14995, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66329] Another function of VGAM1957 is therefore inhibition of T-box 21 (TBX21, Accession NM\_013351). Accordingly,

utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBX21. TPRA40 (Accession NM\_016372) is another VGAM1957 host target gene. TPRA40 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TPRA40, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPRA40 BINDING SITE, designated SEQ ID:18502, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66330] Another function of VGAM1957 is therefore inhibition of TPRA40 (Accession NM\_016372). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPRA40. UDP-glucuronate Decarboxylase 1 (UXS1, Accession NM\_025076) is another VGAM1957 host target gene. UXS1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by UXS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of UXS1 BINDING SITE, designated SEQ ID:24676, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66331] Another function of VGAM1957 is therefore inhibition of UDP-glucuronate Decarboxylase 1 (UXS1, Accession NM\_025076). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UXS1. Xylosyltransferase I (XYLT1, Accession XM\_085432) is another VGAM1957 host target gene. XYLT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XYLT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XYLT1 BINDING SITE, designated SEQ ID:38139, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66332] Another function of VGAM1957 is therefore inhibition of Xylosyltransferase I (XYLT1, Accession XM\_085432). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XYLT1. YF13H12 (Accession NM\_014297)

is another VGAM1957 host target gene. YF13H12 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by YF13H12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YF13H12 BINDING SITE, designated SEQ ID:15594, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66333] Another function of VGAM1957 is therefore inhibition of YF13H12 (Accession NM\_014297). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YF13H12. LOC120114 (Accession XM\_061871) is another VGAM1957 host target gene. LOC120114 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC120114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120114 BINDING SITE, designated SEQ ID:37211, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66334] Another function of VGAM1957 is therefore inhibition of LOC120114 (Accession XM\_061871). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120114. LOC130644 (Accession XM\_065813) is another VGAM1957 host target gene. LOC130644 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130644 BINDING SITE, designated SEQ ID:37303, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66335] Another function of VGAM1957 is therefore inhibition of LOC130644 (Accession XM\_065813). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130644. LOC142955 (Accession XM\_084389) is another VGAM1957 host target gene. LOC142955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC142955, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142955 BINDING SITE, designated SEQ ID:37571, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66336] Another function of VGAM1957 is therefore inhibition of LOC142955 (Accession XM\_084389). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142955. LOC143916 (Accession XM\_084664) is another VGAM1957 host target gene. LOC143916 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143916 BINDING SITE, designated SEQ ID:37652, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66337] Another function of VGAM1957 is therefore inhibition of LOC143916 (Accession XM\_084664). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



LOC143916. LOC145371 (Accession XM\_085123) is another VGAM1957 host target gene. LOC145371 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145371 BINDING SITE, designated SEQ ID:37849, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66338] Another function of VGAM1957 is therefore inhibition of LOC145371 (Accession XM\_085123). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145371. LOC148764 (Accession XM\_086307) is another VGAM1957 host target gene. LOC148764 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148764, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148764 BINDING SITE, designated SEQ ID:38590, to the nucleotide sequence of VGAM1957 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4668.

[66339] Another function of VGAM1957 is therefore inhibition of LOC148764 (Accession XM\_086307). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148764. LOC150577 (Accession XM\_097918) is another VGAM1957 host target gene. LOC150577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150577 BINDING SITE, designated SEQ ID:41222, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66340] Another function of VGAM1957 is therefore inhibition of LOC150577 (Accession XM\_097918). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150577. LOC150967 (Accession XM\_087060) is another VGAM1957 host target gene. LOC150967 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150967, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150967 BINDING SITE, designated SEQ ID:39034, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66341] Another function of VGAM1957 is therefore inhibition of LOC150967 (Accession XM\_087060). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150967. LOC151475 (Accession XM\_098063) is another VGAM1957 host target gene. LOC151475 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151475 BINDING SITE, designated SEQ ID:41358, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66342] Another function of VGAM1957 is therefore inhibition of LOC151475 (Accession XM\_098063). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC151475. LOC157869 (Accession XM\_088409) is another VGAM1957 host target gene. LOC157869 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157869, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157869 BINDING SITE, designated SEQ ID:39677, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66343] Another function of VGAM1957 is therefore inhibition of LOC157869 (Accession XM\_088409). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157869. LOC202025 (Accession XM\_117353) is another VGAM1957 host target gene. LOC202025 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202025 BINDING SITE, designated SEQ ID:43404, to

the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66344] Another function of VGAM1957 is therefore inhibition of LOC202025 (Accession XM\_117353). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202025. LOC255327 (Accession XM\_171236) is another VGAM1957 host target gene. LOC255327 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255327, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255327 BINDING SITE, designated SEQ ID:46022, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66345] Another function of VGAM1957 is therefore inhibition of LOC255327 (Accession XM\_171236). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255327. LOC51336 (Accession NM\_016646) is another VGAM1957 host target gene. LOC51336 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC51336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51336 BINDING SITE, designated SEQ ID:18754, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66346] Another function of VGAM1957 is therefore inhibition of LOC51336 (Accession NM\_016646). Accordingly, utilities of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51336. LOC55971 (Accession NM\_018842) is another VGAM1957 host target gene. LOC55971 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC55971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC55971 BINDING SITE, designated SEQ ID:20827, to the nucleotide sequence of VGAM1957 RNA, herein designated VGAM RNA, also designated SEQ ID:4668.

[66347] Another function of VGAM1957 is therefore inhibition of LOC55971 (Accession NM\_018842). Accordingly, utilities

of VGAM1957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC55971. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1958 (VGAM1958) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[66348] VGAM1958 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1958 was detected is described hereinabove with reference to Figs. 1–8.

[66349] VGAM1958 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1958 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[66350] VGAM1958 gene encodes a VGAM1958 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1958 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1958 precursor RNA is designated SEQ ID:1944, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1944 is located at position 13516 relative to the genome of Macaca Mulatta Rhadinovirus.

[66351] VGAM1958 precursor RNA folds onto itself, forming VGAM1958 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[66352] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1958 folded precursor RNA into VGAM1958 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1958 RNA is designated SEQ ID:4669, and



is provided hereinbelow with reference to the sequence listing part.

[66353] VGAM1958 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1958 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1958 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[66354] VGAM1958 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1958 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1958 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1958 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1958 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[66355] The complementary binding of VGAM1958 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1958 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1958 host target RNA into VGAM1958 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[66356] It is appreciated that VGAM1958 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1958 host target genes. The mRNA of each one of this plurality of VGAM1958 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1958 RNA, herein designated VGAM RNA, and which when bound by VGAM1958 RNA causes inhibition of translation of respective one or more VGAM1958 host target proteins.

[66357] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1958 gene, herein designated VGAM GENE, on one or more VGAM1958 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[66358] It is yet further appreciated that a function of VGAM1958 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1958 correlate with, and may be deduced from, the identity of the host target genes which VGAM1958 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[66359] Nucleotide sequences of the VGAM1958 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1958 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1958 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1958 are further described hereinbelow with reference to Table 1.

[66360] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1958 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1958 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[66361] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1958 gene, herein designated VGAM is inhibition of expression of VGAM1958 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1958 correlate with, and may be deduced from, the identity of the target genes which VGAM1958 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[66362] Amiloride Binding Protein 1 (amine oxidase (copper-containing)) (ABP1, Accession XM\_032220) is a VGAM1958 host target gene. ABP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABP1 BINDING SITE, designated SEQ ID:31613, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66363] A function of VGAM1958 is therefore inhibition of Amiloride Binding Protein 1 (amine oxidase (copper-containing)) (ABP1, Accession XM\_032220), a gene which catalyzes the degradation of compounds such as putrescine. Accordingly, utilities of VGAM1958 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with ABP1. The function of ABP1 has been established by previous studies. Amiloride acts as a diuretic via the closure of epithelial sodium ion channels. Phenamil, an analog of the diuretic amiloride, is a potent blocker of the epithelial sodium channel. Barbry et al. (1990) used phenamil to purify the porcine kidney amiloride-binding protein. They then used synthetic oligonucleotides derived from partial sequences to screen a human kidney cDNA library and to isolate the cDNA encoding the human amiloride-binding protein. Using this cDNA, Barbry et al. (1990) mapped the corresponding structural gene to 7q34-q36 by in situ hybridization. From studies of association between the ABP gene and cystic fibrosis (OMIM Ref. No. 219700) by means of RFLPs, Barbry et al. (1990) excluded the gene from involvement in that disorder. Barbry et al. (1990) pointed out that amiloride-sensitive  $\text{Na}^+$  channels are also present in airway epithelia, where they play an important role in fluid secretion. Amiloride inhibits the excessive absorption of  $\text{Na}^+$  and liquid that takes place in airway epithelia of patients with cystic fibrosis, and amiloride aerosol therapy has been tried for the treatment of lung disease in CF.

[66364] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66365] Barbry, P.; Champe, M.; Chassande, O.; Munemitsu, S.; Champigny, G.; Lingueglia, E.; Maes, P.; Frelin, C.; Tartar, A.; Ullrich, A.; Lazdunski, M. : Human kidney amiloride-binding protein: cDNA structure and functional expression. *Proc. Nat. Acad. Sci.* 87: 7347–7351, 1990. ; and

[66366] Novotny, W. F.; Chassande, O.; Baker, M.; Lazdunski, M.; Barbry, P. : Diamine oxidase is the amiloride-binding protein and is inhibited by amiloride analogues. *J. Biol. Chem.* 269: 9921–9.

[66367] Further studies establishing the function and utilities of ABP1 are found in John Hopkins OMIM database record ID 104610, and in cited publications numbered 202–205 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ACK1 (Accession NM\_005781) is another VGAM1958 host target gene. ACK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ACK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se–

quences of ACK1 BINDING SITE, designated SEQ ID:12358, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66368] Another function of VGAM1958 is therefore inhibition of ACK1 (Accession NM\_005781). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACK1. Adenosine Deaminase, RNA-specific (ADAR, Accession NM\_001111) is another VGAM1958 host target gene. ADAR BINDING SITE1 through ADAR BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADAR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAR BINDING SITE1 through ADAR BINDING SITE3, designated SEQ ID:6773, SEQ ID:17959 and SEQ ID:17966 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66369] Another function of VGAM1958 is therefore inhibition of Adenosine Deaminase, RNA-specific (ADAR, Accession NM\_001111), a gene which converts adenosine to inosine in double-stranded RNA. Accordingly, utilities of



VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAR. The function of ADAR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM323. Adenylate Cyclase 6 (ADCY6, Accession NM\_015270) is another VGAM1958 host target gene. ADCY6 BINDING SITE1 and ADCY6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADCY6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY6 BINDING SITE1 and ADCY6 BINDING SITE2, designated SEQ ID:17588 and SEQ ID:6331 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66370] Another function of VGAM1958 is therefore inhibition of Adenylate Cyclase 6 (ADCY6, Accession NM\_015270), a gene which is a membrane-bound,  $Ca^{2+}$ -inhibitable adenylyl cyclase (by similarity). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY6.

The function of ADCY6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM22. Annexin A5 (ANXA5, Accession NM\_001154) is another VGAM1958 host target gene. ANXA5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ANXA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANXA5 BINDING SITE, designated SEQ ID:6823, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66371] Another function of VGAM1958 is therefore inhibition of Annexin A5 (ANXA5, Accession NM\_001154), a gene which acts as an indirect inhibitor of the thromboplastin-specific complex. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANXA5. The function of ANXA5 has been established by previous studies. PP4 is an anticoagulant protein that acts as an indirect inhibitor of the thromboplastin-specific complex, which is involved in the blood coagulation cascade. It has a relative molecu-

lar weight of about 35,000 and is present in placental tissue to the extent of about 50 mg per placenta with very little secretion into the maternal bloodstream. The PP4 cDNA encoded a protein of 320 amino acid residues. In addition to the PP4 cDNA, Grundmann et al. (1988) identified cDNA encoding a protein with 74% identity to PP4, which they termed PP4-X. PP4 and PP4-X belong to the lipocortin family, as judged by their homology to lipocortin I (OMIM Ref. No. 151690) and calpactin I (OMIM Ref. No. 151720). The placental anticoagulant protein called PAP, isolated by Funakoshi et al. (1987), may be the same protein. PP4 is also known as endonexin II. Endonexin II is a member of the family of  $\text{Ca}^{2+}$ -dependent phospholipid binding proteins, known as annexins, which bind to the phospholipids that are preferentially located on the cytosolic face of the plasma membrane. Kaplan et al. (1988) cloned endonexin II cDNA and expressed it in *Escherichia coli*. A single mRNA, approximately 1.6 kb long, was found to be expressed in human cell lines and placenta. The length of the cDNA clone was 1.59 kb. The cDNA predicted a 320-amino acid protein with a sequence in agreement with the previously determined partial amino acid sequence of endonexin II isolated from placenta.

[66372] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66373] Grundmann, U.; Abel, K.-J.; Bohn, H.; Lobermann, H.; Lottspeich, F.; Kupper, H. : Characterization of cDNA encoding human placental anticoagulant protein (PP4): homology with the lipocortin family. Proc. Nat. Acad. Sci. 85: 3708–3712, 1988. ; and

[66374] Kaplan, R.; Jaye, M.; Burgess, W. H.; Schlaepfer, D. D.; Haigler, H. T. : Cloning and expression of cDNA for human endonexin II, a Ca(2+) and phospholipid binding protein. J. Biol. Chem.

[66375] Further studies establishing the function and utilities of ANXA5 are found in John Hopkins OMIM database record ID 131230, and in cited publications numbered 12203–12210 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Amine Oxidase, Copper Containing 3 (vascular adhesion protein 1) (AOC3, Accession NM\_003734) is another VGAM1958 host target gene. AOC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AOC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AOC3 BINDING SITE, designated SEQ ID:9824, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66376] Another function of VGAM1958 is therefore inhibition of Amine Oxidase, Copper Containing 3 (vascular adhesion protein 1) (AOC3, Accession NM\_003734), a gene which catalyze the oxidative conversion of amines to aldehydes in the presence of copper and quinone cofactor. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AOC3. The function of AOC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM175. Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM\_001282) is another VGAM1958 host target gene. AP2B1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AP2B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP2B1 BIND-

ING SITE, designated SEQ ID:6948, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66377] Another function of VGAM1958 is therefore inhibition of Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM\_001282), a gene which links clathrin to receptors in coated vesicles. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP2B1. The function of AP2B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1126. Ras Homolog Gene Family, Member A (ARHA, Accession XM\_047561) is another VGAM1958 host target gene. ARHA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHA BINDING SITE, designated SEQ ID:35002, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66378] Another function of VGAM1958 is therefore inhibition of Ras Homolog Gene Family, Member A (ARHA, Accession XM\_047561), a gene which regulates remodeling of the actin cytoskeleton during cell morphogenesis and motility. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHA. The function of ARHA has been established by previous studies. The small guanine triphosphatase (GTP) Rho regulates remodeling of the actin cytoskeleton during cell morphogenesis and motility. In their Figure 3C, Maekawa et al. (1999) diagrammed proposed signaling pathways for Rho-induced remodeling of the actin cytoskeleton. They demonstrated that active Rho signals to its downstream effector ROCK1 (OMIM Ref. No. 601702), which phosphorylates and activates LIM kinase (see OMIM Ref. No. 601329). LIM kinase, in turn, phosphorylates cofilin (OMIM Ref. No. 601442), inhibiting its actin-depolymerizing activity. Rao et al. (2001) investigated the role of Rho kinase in the modulation of aqueous humor outflow facility. The treatment of human trabecular meshwork and canal of Schlemm cells with a Rho kinase-specific inhibitor led to significant but reversible changes in cell shape and decreased actin stress fibers, focal ad-

hesions, and protein phosphotyrosine staining. Based on the Rho kinase inhibitor–induced changes in myosin light chain phosphorylation and actomyosin organization, the authors suggested that cellular relaxation and loss of cell–substratum adhesions in the human trabecular meshwork and canal of Schlemm cells could result in either increased paracellular fluid flow across the canal of Schlemm or altered flow pathway through the juxtacanalicular tissue, thereby lowering resistance to outflow. They suggested Rho kinase as a potential target for the development of drugs to modulate intraocular pressure in glaucoma patients.

[66379] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66380] Maekawa, M.; Ishizaki, T.; Boku, S.; Watanabe, N.; Fujita, A.; Iwamatsu, A.; Obinata, T.; Ohashi, K.; Mizuno, K.; Narumiya, S. : Signaling from Rho to the actin cytoskeleton through protein kinases ROCK and LIM–kinase. *Science* 285: 895–898, 1999. ; and

[66381] Rao, P. V.; Deng, P.–F.; Kumar, J.; Epstein, D. L. : Modulation of aqueous humor outflow facility by the Rho kinase–specific inhibitor Y–27632. *Invest. Ophthalm. Vis. Sci.* 42:



1029–1037.

[66382] Further studies establishing the function and utilities of ARHA are found in John Hopkins OMIM database record ID 165390, and in cited publications numbered 10904, 1090 and 10911–10913 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rho Guanine Nucleotide Exchange Factor (GEF) 7 (ARHGEF7, Accession NM\_003899) is another VGAM1958 host target gene. ARHGEF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF7 BINDING SITE, designated SEQ ID:9981, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66383] Another function of VGAM1958 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 7 (ARHGEF7, Accession NM\_003899), a gene which acts as a rac1 guanine nucleotide exchange factor (gef) and can induce membrane ruffling. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ARHGEF7. The function of ARHGEF7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM297. Arylsulfatase B (ARSB, Accession NM\_000046) is another VGAM1958 host target gene. ARSB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARSB BINDING SITE, designated SEQ ID:5488, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66384] Another function of VGAM1958 is therefore inhibition of Arylsulfatase B (ARSB, Accession NM\_000046). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARSB. Armadillo Repeat Gene Deletes In Velocardiofacial Syndrome (ARVCF, Accession NM\_001670) is another VGAM1958 host target gene. ARVCF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARVCF, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARVCF BINDING SITE, designated SEQ ID:7383, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66385] Another function of VGAM1958 is therefore inhibition of Armadillo Repeat Gene Deletes In Velocardiofacial Syndrome (ARVCF, Accession NM\_001670), a gene which is involved in protein-protein interactions at adherens junctions. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARVCF. The function of ARVCF has been established by previous studies. Velocardiofacial syndrome (VCFS; 192430) and DiGeorge syndrome (DGS; 188400) are autosomal dominant disorders that share a wide spectrum of phenotypes, including cleft palate, conotruncal heart defects, and facial dysmorphology. Both syndromes are thought to result from a developmental field defect. Hemizygosity for a portion of 22q11 has been detected in 80 to 85% of VCFS/DGS patients. To identify genes in 22q11 that may contribute to the phenotype of VCFS, Sirotkin et al. (1997) used cDNA selection and cDNA

library screening to clone the full-length human 'armadillo repeat gene deleted in VCFS' (ARVCF) cDNA. ARVCF encodes a 962-amino acid protein that contains 2 motifs involved in protein-protein interactions: a coiled-coil domain near the N terminus and 10 tandem armadillo repeats in the central region. Comparison of the ARVCF sequence with protein databases showed that the structure of ARVCF is most closely related to the catenin family. Members of this family play important roles in the formation of adherens junction complexes. These data suggest that ARVCF is involved in protein-protein interactions at adherens junctions. Unlike other catenin family members, ARVCF contains a nuclear localization signal (NLS), suggesting that ARVCF functions as a nuclear protein. Northern blotting showed that ARVCF is ubiquitously expressed as a 4.0- to 4.3-kb transcript in fetal and adult tissues, and Southern blotting revealed that ARVCF is conserved in vertebrates and *Drosophila*. Sirotkin et al. (1997) mapped the ARVCF gene to chromosome 22 by fluorescence in situ hybridization and to 22q11 using physical mapping methods. ARVCF is located within the region of 22q11 that is hemizygous in all VCFS/DGS patients who have interstitial deletions. Based on the physical location and potential

functions of ARVCF, Sirotkin et al. (1997) suggested that hemizyosity of ARVCF plays a role in the etiology of some of the phenotypes associated with VCFS.

[66386] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66387] Bonne, S.; van Hengel, J.; van Roy, F. : Chromosomal mapping of human armadillo genes belonging to the p120(ctn)/plakophilin subfamily. *Genomics* 51: 452–454, 1998. ; and

[66388] Sirotkin, H.; O'Donnell, H.; DasGupta, R.; Halford, S.; St. Jore, B.; Puech, A.; Parimoo, S.; Morrow, B.; Skoultchi, A.; Weissman, S. M.; Scambler, P.; Kucherlapati, R. : Identification.

[66389] Further studies establishing the function and utilities of ARVCF are found in John Hopkins OMIM database record ID 602269, and in cited publications numbered 702 and 8675 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATPase, Class VI, Type 11A (ATP11A, Accession XM\_085028) is another VGAM1958 host target gene. ATP11A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP11A, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP11A BINDING SITE, designated SEQ ID:37807, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66390] Another function of VGAM1958 is therefore inhibition of ATPase, Class VI, Type 11A (ATP11A, Accession XM\_085028). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP11A. ATPase, Cu<sup>++</sup> Transporting, Beta Polypeptide (Wilson disease) (ATP7B, Accession NM\_000053) is another VGAM1958 host target gene. ATP7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP7B BINDING SITE, designated SEQ ID:5506, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66391] Another function of VGAM1958 is therefore inhibition of

ATPase, Cu++ Transporting, Beta Polypeptide (Wilson disease) (ATP7B, Accession NM\_000053). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP7B. ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM\_036933) is another VGAM1958 host target gene. ATP8B2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ATP8B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8B2 BINDING SITE, designated SEQ ID:32516, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66392] Another function of VGAM1958 is therefore inhibition of ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM\_036933). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8B2. Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession NM\_000489) is another VGAM1958 host target gene. ATRX BINDING SITE1

and ATRX BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ATRX, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATRX BINDING SITE1 and ATRX BINDING SITE2, designated SEQ ID:6093 and SEQ ID:28681 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66393] Another function of VGAM1958 is therefore inhibition of Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession NM\_000489). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATRX. Beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_054025) is another VGAM1958 host target gene. B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GAT1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of



B3GAT1 BINDING SITE1 and B3GAT1 BINDING SITE2, designated SEQ ID:27628 and SEQ ID:20716 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66394] Another function of VGAM1958 is therefore inhibition of Beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1, Accession NM\_054025). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GAT1. UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 2 (B4GALT2, Accession NM\_003780) is another VGAM1958 host target gene. B4GALT2 BINDING SITE1 and B4GALT2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B4GALT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT2 BINDING SITE1 and B4GALT2 BINDING SITE2, designated SEQ ID:9865 and SEQ ID:6860 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66395] Another function of VGAM1958 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 2 (B4GALT2, Accession NM\_003780). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT2. Bassoon (presynaptic cytomatrix protein) (BSN, Accession NM\_003458) is another VGAM1958 host target gene. BSN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BSN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BSN BINDING SITE, designated SEQ ID:9520, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66396] Another function of VGAM1958 is therefore inhibition of Bassoon (presynaptic cytomatrix protein) (BSN, Accession NM\_003458), a gene which may be involved in cytomatrix organization at the site of neurotransmitter release. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BSN. The function of BSN and its associa-

tion with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM638. Calcium Channel, Voltage-dependent, Alpha 2/delta Subunit 2 (CACNA2D2, Accession NM\_006030) is another VGAM1958 host target gene. CACNA2D2 BINDING SITE1 and CACNA2D2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CACNA2D2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNA2D2 BINDING SITE1 and CACNA2D2 BINDING SITE2, designated SEQ ID:12651 and SEQ ID:12648 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66397] Another function of VGAM1958 is therefore inhibition of Calcium Channel, Voltage-dependent, Alpha 2/delta Subunit 2 (CACNA2D2, Accession NM\_006030), a gene which is a calcium channel protein which plays an important role in excitation-contraction coupling. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNA2D2. The function of CACNA2D2 and its associa-

tion with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM203. CARPX (Accession NM\_020178) is another VGAM1958 host target gene. CARPX BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CARPX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARPX BINDING SITE, designated SEQ ID:21395, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66398] Another function of VGAM1958 is therefore inhibition of CARPX (Accession NM\_020178), a gene which is alpha-carbonic anhydrases-related protein. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARPX. The function of CARPX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM904. Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM\_001228) is another

VGAM1958 host target gene. CASP8 BINDING SITE1 and CASP8 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CASP8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP8 BINDING SITE1 and CASP8 BINDING SITE2, designated SEQ ID:6897 and SEQ ID:27210 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66399] Another function of VGAM1958 is therefore inhibition of Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM\_001228), a gene which is an apoptosis-related caspase and an upstream component of Fas receptor and tumor necrosis factor (TNF) receptor-induced apoptosis. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP8. The function of CASP8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM145.CD80 Antigen (CD28 antigen ligand 1, B7-1 antigen) (CD80, Ac-

cession NM\_005191) is another VGAM1958 host target gene. CD80 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CD80, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD80 BINDING SITE, designated SEQ ID:11695, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66400] Another function of VGAM1958 is therefore inhibition of CD80 Antigen (CD28 antigen ligand 1, B7-1 antigen) (CD80, Accession NM\_005191), a gene which provides regulatory signals for T lymphocytes. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD80. The function of CD80 has been established by previous studies. The B-lymphocyte activation antigen B7-1 (formerly referred to as B7) provides regulatory signals for T lymphocytes as a consequence of binding to the CD28 (OMIM Ref. No. 186760) and CTLA-4 (OMIM Ref. No. 123890) ligands of T cells. The cDNA for B7-1 predicts a type I membrane protein, i.e., one synthesized with a signal peptide that is cleaved upon translocation across the

endoplasmic membrane. The protein is predicted to contain 2 extracellular domains structurally similar to those of Ig, a hydrophobic transmembrane region, and a short cytoplasmic domain. Selvakumar et al. (1992) found that the gene has 6 exons that span approximately 32 kb of genomic DNA. Exon 1 is not translated, and exon 2 contains the initiation ATG codon and encodes a predicted signal peptide. Exons 3 and 4 correspond to 2 Ig-like domains, whereas exons 5 and 6, respectively, encode the transmembrane portion and the cytoplasmic tail. This close relationship between exons and functional domains is a characteristic feature of genes of the Ig superfamily. As the ligand for CD28, LAB7-1 is also symbolized CD28LG1. Reeves et al. (1997) demonstrated that the CD80 and CD86 (OMIM Ref. No. 601020) genes are linked on human chromosome 3 and mouse chromosome 16. These 2 genes encode B7-1 and B7-2, respectively, which are structurally similar members of the immunoglobulin superfamily expressed on a variety of hematopoietic cell types. Reeves et al. (1997) stated that they provide a costimulatory signal to T cells by interacting with CD28 and CTLA4

[66401] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [66402] Selvakumar, A.; Mohanraj, B. K.; Eddy, R. L.; Shows, T. B.; White, P. C.; Dupont, B. : Genomic organization and chromosomal location of the human gene encoding the B-lymphocyte activation antigen B7. Immunogenetics 36: 175-181, 1992. ; and
- [66403] Reeves, R. H.; Patch, D.; Sharpe, A. H.; Borriello, F.; Freeman, G. J.; Edelhoff, S.; Disteché, C. : The costimulatory genes Cd80 and Cd86 are linked on mouse chromosome 16 and human chr.
- [66404] Further studies establishing the function and utilities of CD80 are found in John Hopkins OMIM database record ID 112203, and in cited publications numbered 4548, 4549-455 and 4346 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CD83 Antigen (activated B lymphocytes, immunoglobulin superfamily) (CD83, Accession NM\_004233) is another VGAM1958 host target gene. CD83 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD83, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-



trates the complementarity of the nucleotide sequences of CD83 BINDING SITE, designated SEQ ID:10426, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66405] Another function of VGAM1958 is therefore inhibition of CD83 Antigen (activated B lymphocytes, immunoglobulin superfamily) (CD83, Accession NM\_004233), a gene which may play a significant role in antigen presentation or the cellular interactions that follow lymphocyte activation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD83. The function of CD83 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1929. Cadherin Related 23 (CDH23, Accession NM\_022124) is another VGAM1958 host target gene. CDH23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH23 BINDING SITE, designated SEQ ID:22669, to the nucleotide sequence of

VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66406] Another function of VGAM1958 is therefore inhibition of Cadherin Related 23 (CDH23, Accession NM\_022124). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH23. Cyclin-dependent Kinase Inhibitor 1A (p21, Cip1) (CDKN1A, Accession NM\_078467) is another VGAM1958 host target gene. CDKN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDKN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN1A BINDING SITE, designated SEQ ID:27781, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66407] Another function of VGAM1958 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 1A (p21, Cip1) (CDKN1A, Accession NM\_078467), a gene which inhibits cyclin-kinase activity and probably serves as the effector of p53 cell cycle control. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CDKN1A. The function of CDKN1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1912. Centromere Protein B, 80kDa (CENPB, Accession XM\_045451) is another VGAM1958 host target gene. CENPB BINDING SITE1 and CENPB BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CENPB, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENPB BINDING SITE1 and CENPB BINDING SITE2, designated SEQ ID:34463 and SEQ ID:34466 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66408] Another function of VGAM1958 is therefore inhibition of Centromere Protein B, 80kDa (CENPB, Accession XM\_045451), a gene which is the major centromere antigen . Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENPB. The function of CENPB and its association with various diseases and clinical condi-

tions, has been established by previous studies, as described hereinabove with reference to VGAM206. Centrosomal Protein 2 (CEP2, Accession NM\_007186) is another VGAM1958 host target gene. CEP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CEP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP2 BINDING SITE, designated SEQ ID:14042, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66409] Another function of VGAM1958 is therefore inhibition of Centrosomal Protein 2 (CEP2, Accession NM\_007186), a gene which interacts with TC10 and CDC42. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEP2. The function of CEP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM329. Cholinergic Receptor, Nicotinic, Beta Polypeptide 1 (muscle) (CHRNA1, Accession XM\_018451) is another VGAM1958 host target gene.

CHRNA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRNA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRNA1 BINDING SITE, designated SEQ ID:30360, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66410] Another function of VGAM1958 is therefore inhibition of Cholinergic Receptor, Nicotinic, Beta Polypeptide 1 (muscle) (CHRNA1, Accession XM\_018451). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRNA1. Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 5 (CHST5, Accession NM\_012126) is another VGAM1958 host target gene. CHST5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHST5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST5 BINDING SITE, designated SEQ ID:14439, to the nucleotide se-

quence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66411] Another function of VGAM1958 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 5 (CHST5, Accession NM\_012126), a gene which may be involved in sulfation of glycoproteins and proteoglycans. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST5. The function of CHST5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM186. Chloride Channel 7 (CLCN7, Accession NM\_001287) is another VGAM1958 host target gene. CLCN7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLCN7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN7 BINDING SITE, designated SEQ ID:6964, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66412] Another function of VGAM1958 is therefore inhibition of

Chloride Channel 7 (CLCN7, Accession NM\_001287), a gene which is voltage-gated chloride channel. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCN7. The function of CLCN7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM623.C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252) is another VGAM1958 host target gene. CLECSF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLECSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF5 BINDING SITE, designated SEQ ID:14919, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66413] Another function of VGAM1958 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM\_013252). Accordingly, utilities of VGAM1958 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF5. Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM\_033096) is another VGAM1958 host target gene. CLTCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLTCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLTCL1 BINDING SITE, designated SEQ ID:31838, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66414] Another function of VGAM1958 is therefore inhibition of Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM\_033096), a gene which is involved in vesicle budding. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLTCL1. The function of CLTCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42. Collagen, Type XI, Alpha 2 (COL11A2, Accession NM\_080681) is another VGAM1958 host target gene. COL11A2 BINDING



SITE1 and COL11A2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL11A2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL11A2 BINDING SITE1 and COL11A2 BINDING SITE2, designated SEQ ID:27979 and SEQ ID:27974 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66415] Another function of VGAM1958 is therefore inhibition of Collagen, Type XI, Alpha 2 (COL11A2, Accession NM\_080681). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL11A2. Collagen-like Tail Subunit (single strand of homotrimer) of Asymmetric Acetylcholinesterase (COLQ, Accession NM\_080539) is another VGAM1958 host target gene. COLQ BINDING SITE1 through COLQ BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COLQ, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of COLQ BINDING SITE1 through COLQ BINDING SITE6, designated SEQ ID:27855, SEQ ID:27858, SEQ ID:27864, SEQ ID:27852, SEQ ID:27861 and SEQ ID:12232 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66416] Another function of VGAM1958 is therefore inhibition of Collagen-like Tail Subunit (single strand of homotrimer) of Asymmetric Acetylcholinesterase (COLQ, Accession NM\_080539). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COLQ. Copine VII (CPNE7, Accession NM\_014427) is another VGAM1958 host target gene. CPNE7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPNE7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPNE7 BINDING SITE, designated SEQ ID:15787, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66417] Another function of VGAM1958 is therefore inhibition of

Copine VII (CPNE7, Accession NM\_014427). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPNE7. Cofactor Required For Sp1 Transcriptional Activation, Subunit 6, 77kDa (CRSP6, Accession NM\_004268) is another VGAM1958 host target gene. CRSP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CRSP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRSP6 BINDING SITE, designated SEQ ID:10471, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66418] Another function of VGAM1958 is therefore inhibition of Cofactor Required For Sp1 Transcriptional Activation, Subunit 6, 77kDa (CRSP6, Accession NM\_004268), a gene which is required for Sp1 mediated transcriptional activation with TAF(II)s. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRSP6. The function of CRSP6 has been established by previous studies. Using a

HeLa cell line, Ito et al. (1999) cloned TRAP80, the gene encoding the 80-kD subunit of the TRAP complex. (For background information on thyroid hormone receptor-associated proteins (TRAPs), see 300182). The TRAP80 cDNA encodes a 717-amino acid protein that has no obvious motifs other than a short leucine zipper in the middle of the sequence. The TRAP80 cDNA appears to be equivalent to the p78 component of the mouse Mediator (Jiang et al., 1998). Northern blot analysis of multiple human tissues showed that the TRAP80 gene is ubiquitously expressed as an approximately 3.0-kb transcript. Gene transcription requires factors that recognize transcriptional enhancer sites in DNA. These factors work with coactivators to direct transcriptional initiation by the RNA polymerase II apparatus (see OMIM Ref. No. POLR2A, 180660). Transcriptional activation by enhancer-binding factors such as SP1 (OMIM Ref. No. 189906) requires interaction with the TFIID complex (see OMIM Ref. No. TAF2A, 313650). To identify other potential SP1 cofactors, Ryu et al. (1999) developed an in vitro transcription assay consisting of TFIIA (GTF2A1; 600520), RNA polII, and the basal transcription factors GTF2B (OMIM Ref. No. 189963), GTF2E (OMIM Ref. No. 189962), GTF2F (OMIM Ref. No.

189968), and GTF2H (OMIM Ref. No. 189972), supplemented with TFIID or TBP (OMIM Ref. No. 600075). By sequential chromatography, they excluded PC4 (OMIM Ref. No. 600503) as an SP1 cofactor and identified a multisubunit cofactor, CRSP (cofactor required for SP1 activation), which, along with TFIID, is required for efficient activation by SP1. CRSP behaves as a single complex of approximately 700 kD. Ryu et al. (1999) tentatively identified 9 polypeptides as CRSP subunits (see OMIM Ref. No. also PPARBP, 604311). Using microsequence peptide analysis, they cloned a CRSP cDNA encoding a 77-kD protein, CRSP6, which they termed CRSP77

[66419] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66420] Ito, M.; Yuan, C.-X.; Malik, S.; Gu, W.; Fondell, J. D.; Yamamura, S.; Fu, Z.-Y.; Zhang, X.; Qin, J.; Roeder, R. G. : Identity between TRAP and SMCC complexes indicates novel pathways for the function of nuclear receptors and diverse mammalian activators. *Molec. Cell* 3: 361-370, 1999. ; and

[66421] Ryu, S.; Zhou, S.; Ladurner, A. G.; Tjian, R. : The transcriptional cofactor complex CRSP is required for activity of the

enhancer-binding protein Sp1. Nature 397: 446–450, 1999.

[66422] Further studies establishing the function and utilities of CRSP6 are found in John Hopkins OMIM database record ID 603810, and in cited publications numbered 11384 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cysteine and Glycine-rich Protein 1 (CSRP1, Accession NM\_004078) is another VGAM1958 host target gene. CSRP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSRP1 BINDING SITE, designated SEQ ID:10277, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66423] Another function of VGAM1958 is therefore inhibition of Cysteine and Glycine-rich Protein 1 (CSRP1, Accession NM\_004078), a gene which could play a role in neuronal development. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSRP1. The function of

CSRP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM743. Cathepsin D (lysosomal aspartyl protease) (CTSD, Accession NM\_001909) is another VGAM1958 host target gene. CTSD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTSD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTSD BINDING SITE, designated SEQ ID:7627, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66424] Another function of VGAM1958 is therefore inhibition of Cathepsin D (lysosomal aspartyl protease) (CTSD, Accession NM\_001909). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTSD. Cullin 4B (CUL4B, Accession NM\_003588) is another VGAM1958 host target gene. CUL4B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CUL4B, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CUL4B BINDING SITE, designated SEQ ID:9639, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66425] Another function of VGAM1958 is therefore inhibition of Cullin 4B (CUL4B, Accession NM\_003588), a gene which is a negative regulator of the cell cycle in *C. elegans*. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CUL4B. The function of CUL4B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM140. Chemokine (C-X-C motif) Ligand 16 (CXCL16, Accession NM\_022059) is another VGAM1958 host target gene. CXCL16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXCL16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXCL16 BINDING SITE, designated SEQ ID:22600, to the nucleotide



sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66426] Another function of VGAM1958 is therefore inhibition of Chemokine (C-X-C motif) Ligand 16 (CXCL16, Accession NM\_022059), a gene which induces calcium mobilization. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXCL16. The function of CXCL16 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1845. Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 1 (CYP1A1, Accession NM\_000499) is another VGAM1958 host target gene. CYP1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP1A1 BINDING SITE, designated SEQ ID:6112, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66427] Another function of VGAM1958 is therefore inhibition of Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 1 (CYP1A1, Accession NM\_000499), a gene which intervenes in an NADPH-dependent electron transport pathway. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP1A1. The function of CYP1A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM335. Cytochrome P450, Subfamily I (dioxin-inducible), Polypeptide 1 (glaucoma 3, primary infantile) (CYP1B1, Accession NM\_000104) is another VGAM1958 host target gene. CYP1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP1B1 BINDING SITE, designated SEQ ID:5564, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66428] Another function of VGAM1958 is therefore inhibition of

Cytochrome P450, Subfamily I (dioxin-inducible), Polypeptide 1 (glaucoma 3, primary infantile) (CYP1B1, Accession NM\_000104), a gene which participates in the metabolism of a molecule that is a participant in eye development. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP1B1. The function of CYP1B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM894.

Cytochrome P450, Subfamily XXVIIIB (25-hydroxyvitamin D-1-alpha-hydroxylase), Polypeptide 1 (CYP27B1, Accession NM\_000785) is another VGAM1958 host target gene. CYP27B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP27B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP27B1 BINDING SITE, designated SEQ ID:6432, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66429] Another function of VGAM1958 is therefore inhibition of

Cytochrome P450, Subfamily XXVIIB (25-hydroxyvitamin D-1-alpha-hydroxylase), Polypeptide 1 (CYP27B1, Accession NM\_000785). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP27B1. Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM\_004393) is another VGAM1958 host target gene. DAG1 BINDING SITE1 and DAG1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DAG1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAG1 BINDING SITE1 and DAG1 BINDING SITE2, designated SEQ ID:10630 and SEQ ID:10634 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66430] Another function of VGAM1958 is therefore inhibition of Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM\_004393), a gene which may provide linkage between the sarcolemma and extracellular matrix (ECM). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with DAG1. The function of DAG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1095.DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 11 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX11, Accession NM\_004399) is another VGAM1958 host target gene. DDX11 BINDING SITE1 and DDX11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DDX11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX11 BINDING SITE1 and DDX11 BINDING SITE2, designated SEQ ID:10653 and SEQ ID:24986 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66431] Another function of VGAM1958 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 11 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX11, Accession NM\_004399), a gene which could be an ATP-dependent DNA-binding helicase and may intervene in cell cycle regulation. Accordingly, utilities of VGAM1958

include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX11. The function of DDX11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1533. Dihydrofolate Reductase (DHFR, Accession NM\_000791) is another VGAM1958 host target gene. DHFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DHFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DHFR BINDING SITE, designated SEQ ID:6450, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66432] Another function of VGAM1958 is therefore inhibition of Dihydrofolate Reductase (DHFR, Accession NM\_000791), a gene which converts dihydrofolate into tetrahydrofolate. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DHFR. The function of DHFR and its association with various diseases and clinical conditions, has been established by previous studies, as described

hereinabove with reference to VGAM826. Dystrophia Myotonica-protein Kinase (DMPK, Accession NM\_004409) is another VGAM1958 host target gene. DMPK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DMPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMPK BINDING SITE, designated SEQ ID:10666, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66433] Another function of VGAM1958 is therefore inhibition of Dystrophia Myotonica-protein Kinase (DMPK, Accession NM\_004409). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMPK. DnaJ (Hsp40) Homolog, Subfamily B, Member 1 (DNAJB1, Accession NM\_006145) is another VGAM1958 host target gene. DNAJB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of DNAJB1 BINDING SITE, designated SEQ ID:12787, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66434] Another function of VGAM1958 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily B, Member 1 (DNAJB1, Accession NM\_006145), a gene which may prevent aggregation of newly translated proteins. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJB1. The function of DNAJB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1778. Diphtheria Toxin Resistance Protein Required For Diphthamide Biosynthesis-like 1 (*S. cerevisiae*) (DPH2L1, Accession NM\_001383) is another VGAM1958 host target gene. DPH2L1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DPH2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPH2L1 BINDING SITE, designated SEQ ID:7054, to the nucleotide



sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66435] Another function of VGAM1958 is therefore inhibition of Diphtheria Toxin Resistance Protein Required For Diphthamide Biosynthesis-like 1 (*S. cerevisiae*) (DPH2L1, Accession NM\_001383), a gene which may be involved in regulating global protein synthesis; has similarity to *S. cerevisiae* Dph2p. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPH2L1. The function of DPH2L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM608. Dystrobrevin, Alpha (DTNA, Accession NM\_001391) is another VGAM1958 host target gene. DTNA BINDING SITE1 through DTNA BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DTNA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DTNA BINDING SITE1 through DTNA BINDING SITE4, designated SEQ ID:7082, SEQ ID:26844, SEQ ID:26839 and SEQ ID:26849 respec-

tively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66436] Another function of VGAM1958 is therefore inhibition of Dystrobrevin, Alpha (DTNA, Accession NM\_001391), a gene which may be involved in the formation and stability of synapses. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DTNA. The function of DTNA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1021. Ectodermal Dysplasia 1, Anhidrotic (ED1, Accession NM\_001399) is another VGAM1958 host target gene. ED1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ED1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ED1 BINDING SITE, designated SEQ ID:7098, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66437] Another function of VGAM1958 is therefore inhibition of

Ectodermal Dysplasia 1, Anhidrotic (ED1, Accession NM\_001399). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ED1. Ephrin-A3 (EFNA3, Accession NM\_004952) is another VGAM1958 host target gene. EFNA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNA3 BINDING SITE, designated SEQ ID:11394, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66438] Another function of VGAM1958 is therefore inhibition of Ephrin-A3 (EFNA3, Accession NM\_004952), a gene which is a ligand of Eph-related receptor tyrosine kinases. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNA3. The function of EFNA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1929.EGF-like-domain,

Multiple 6 (EGFL6, Accession NM\_015507) is another VGAM1958 host target gene. EGFL6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGFL6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL6 BINDING SITE, designated SEQ ID:17765, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66439] Another function of VGAM1958 is therefore inhibition of EGF-like-domain, Multiple 6 (EGFL6, Accession NM\_015507), a gene which is a members of the epidermal growth factor (EGF) repeat superfamily which are often involved in the regulation of cell cycle, proliferation, and developmental processes. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL6. The function of EGFL6 has been established by previous studies. Using a high-throughput screening-by-hybridization approach, Yeung et al. (1999) identified the EGFL6 gene. The predicted 553-amino acid EGFL6 protein has a putative N-terminal signal peptide, which

suggests that it is secreted; an EGF repeat region containing 4 complete EGF-like repeats and 1 partial EGF-like repeat; an integrin association motif (RGD); 2 potential N-glycosylation sites; and a potential tyrosine phosphorylation site. Northern blot analysis of a variety of normal human tissues detected an approximately 2.4-kb EGFL6 transcript only in placenta. Among the cancer tissues tested, EGFL6 expression was found only in meningioma tumors. Screening-by-hybridization analysis of various cDNA libraries indicated EGFL6 expression in lung tumor, fetal lung, fetal skin, fetal umbilical cord, fetal liver/spleen, and placenta, but not in normal adult tissues, including lung. Buchner et al. (2000) determined that the MAEG gene contains 12 exons.

[66440] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66441] Yeung, G.; Mulero, J. J.; Berntsen, R. P.; Loeb, D. B.; Drmanac, R.; Ford, J. E. : Cloning of a novel epidermal growth factor repeat containing gene EGFL6: expressed in tumor and fetal tissues. *Genomics* 62: 304-307, 1999. ; and

[66442] Buchner, G.; Orfanelli, U.; Quaderi, N.; Bassi, M. T.; An-

dolfi, G.; Ballabio, A.; Franco, B. : Identification of a new EGF-repeat-containing gene from human Xp22: a candidate for develo.

[66443] Further studies establishing the function and utilities of EGFL6 are found in John Hopkins OMIM database record ID 300239, and in cited publications numbered 9013–9014 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Egl Nine Homolog 1 (C. elegans) (EGLN1, Accession NM\_022051) is another VGAM1958 host target gene. EGLN1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by EGLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGLN1 BINDING SITE, designated SEQ ID:22579, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66444] Another function of VGAM1958 is therefore inhibition of Egl Nine Homolog 1 (C. elegans) (EGLN1, Accession NM\_022051), a gene which is expressed in the cytoplasm of arterial smooth muscle cells. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with EGLN1. The function of EGLN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM216. Egl Nine Homolog 2 (*C. elegans*) (EGLN2, Accession NM\_017555) is another VGAM1958 host target gene. EGLN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGLN2 BINDING SITE, designated SEQ ID:18991, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66445] Another function of VGAM1958 is therefore inhibition of Egl Nine Homolog 2 (*C. elegans*) (EGLN2, Accession NM\_017555), a gene which is an essential component of the pathway. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGLN2. The function of EGLN2 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM432.Egl Nine Homolog 3 (*C. elegans*) (EGLN3, Accession NM\_022073) is another VGAM1958 host target gene. EGLN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGLN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGLN3 BINDING SITE, designated SEQ ID:22618, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66446] Another function of VGAM1958 is therefore inhibition of Egl Nine Homolog 3 (*C. elegans*) (EGLN3, Accession NM\_022073), a gene which is an essential component of the pathway. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGLN3. The function of EGLN3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206.EH-domain Containing 4 (EHD4, Accession NM\_139265) is another VGAM1958 host target gene.



EHD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EHD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EHD4 BINDING SITE, designated SEQ ID:29254, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66447] Another function of VGAM1958 is therefore inhibition of EH-domain Containing 4 (EHD4, Accession NM\_139265). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EHD4. Eukaryotic Translation Initiation Factor 4A, Isoform 2 (EIF4A2, Accession NM\_001967) is another VGAM1958 host target gene. EIF4A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF4A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4A2 BINDING SITE, designated SEQ ID:7696, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66448] Another function of VGAM1958 is therefore inhibition of Eukaryotic Translation Initiation Factor 4A, Isoform 2 (EIF4A2, Accession NM\_001967), a gene which is a sub-unit of a high molecular weight protein complex and is required as a single polypeptide chain for mrna binding to ribosome. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF4A2. The function of EIF4A2 has been established by previous studies. Eukaryotic initiation factor 4A plays an important role in the binding of mRNA to the 43S preinitiation complex when protein synthesis begins. Two highly homologous forms of functional EIF4A genes, Eif4a1 (OMIM Ref. No. 602641) and Eif4a2, have been isolated in mice (Nielsen and Trachsel, 1988); yeast cells also possess 2 EIF4A genes, TIF1 and TIF2 (OMIM Ref. No. 601993). The murine Eif4a and yeast TIF genes appear to belong to a DEAD-box gene family, whose members exhibit extensive amino acid similarity and contain the asp-glu-ala-asp (DEAD) sequence. DEAD-box genes have been identified in species ranging from E-coli to humans. Their function appears to be related to transcriptional/translational regulation. Sudo et al. (1995) isolated human cDNA highly homologous to murine

Eif4a2, which encodes one of the protein-synthesis initiation factors involved in the binding of mRNA to the ribosome. The human homolog was expressed in all normal tissues examined, but in variable amounts, being highly expressed in skeletal muscle and ovary, and less abundantly in liver, kidney, and pancreas.

[66449] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66450] Nielsen, P. J.; Trachsel, H. : The mouse protein synthesis initiation factor 4A gene family includes two related functional genes which are differentially expressed. EMBO J. 7: 2097-2105, 1988. ; and

[66451] Sudo, K.; Takahashi, E.; Nakamura, Y. : Isolation and mapping of the human EIF4A2 gene homologous to the murine protein synthesis initiation factor 4A-II gene Eif4a2. Cytogenet. Cell Ge.

[66452] Further studies establishing the function and utilities of EIF4A2 are found in John Hopkins OMIM database record ID 601102, and in cited publications numbered 9632-9634 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ELL (Accession NM\_006532) is another VGAM1958 host target

gene. ELL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELL BINDING SITE, designated SEQ ID:13280, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66453] Another function of VGAM1958 is therefore inhibition of ELL (Accession NM\_006532). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELL. Ectonucleoside Triphosphate Diphosphohydrolase 6 (putative function) (ENTPD6, Accession NM\_001247) is another VGAM1958 host target gene. ENTPD6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENTPD6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENTPD6 BINDING SITE, designated SEQ ID:6918, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66454] Another function of VGAM1958 is therefore inhibition of Ectonucleoside Triphosphate Diphosphohydrolase 6 (putative function) (ENTPD6, Accession NM\_001247), a gene which might support glycosylation reactions in the golgi apparatus and, when released from cells, might catalyze the hydrolysis of extracellular nucleotides. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENTPD6. The function of ENTPD6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827.E1A Binding Protein P300 (EP300, Accession NM\_001429) is another VGAM1958 host target gene. EP300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EP300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EP300 BINDING SITE, designated SEQ ID:7149, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66455] Another function of VGAM1958 is therefore inhibition of

E1A Binding Protein P300 (EP300, Accession NM\_001429), a gene which may have a function in cell cycle regulation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EP300. The function of EP300 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Erythrocyte Membrane Protein Band 4.9 (dematin) (EPB49, Accession NM\_001978) is another VGAM1958 host target gene. EPB49 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EPB49, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB49 BINDING SITE, designated SEQ ID:7709, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66456] Another function of VGAM1958 is therefore inhibition of Erythrocyte Membrane Protein Band 4.9 (dematin) (EPB49, Accession NM\_001978), a gene which is an actin-bundling protein. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with EPB49. The function of EPB49 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM760. Epilepsy, Progressive Myoclonus Type 2, Lafora Disease (laforin) (EPM2A, Accession NM\_005670) is another VGAM1958 host target gene. EPM2A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EPM2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPM2A BINDING SITE, designated SEQ ID:12226, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66457] Another function of VGAM1958 is therefore inhibition of Epilepsy, Progressive Myoclonus Type 2, Lafora Disease (laforin) (EPM2A, Accession NM\_005670), a gene which Laforin; protein tyrosine phosphatase that may have role in glycogen metabolism. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPM2A. The function of EPM2A and its association with various

diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM470.V-ets Erythroblastosis Virus E26 Oncogene Homolog 2 (avian) (ETS2, Accession NM\_005239) is another VGAM1958 host target gene. ETS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ETS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ETS2 BINDING SITE, designated SEQ ID:11748, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66458] Another function of VGAM1958 is therefore inhibition of V-ets Erythroblastosis Virus E26 Oncogene Homolog 2 (avian) (ETS2, Accession NM\_005239), a gene which Transcription factor. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ETS2. The function of ETS2 has been established by previous studies. See 164720. By in situ hybridization, Watson et al. (1985) mapped the ETS2 locus to 21q22.1-q22.3. Sacchi et al. (1986) found that the ETS2 gene was translocated to



chromosome 8 in the translocation t(8;21)(q22;q22), which is commonly found in patients with acute myeloid leukemia with morphology M2 (OMIM Ref. No. AML-M2). In a case of t(8;21)(q22;q22), Le Beau et al. (1986) found that the ETS2 gene was translocated to chromosome 8. The MOS oncogene (OMIM Ref. No. 190060) was retained at the breakpoint on chromosome 8; thus, one or both of these genes may play a role in the pathogenesis of acute myelogenous leukemia. Using genetic linkage analysis, Sacchi et al. (1988) demonstrated the location of the ETS2 gene relative to other loci and established that the breakpoint in acute myeloid leukemia is about 17 cM from ETS2. Thus, the breakpoint does not affect the ETS2 gene structure. The actual DNA sequence involved in the t(8;21) may reside in a 3-cM genetic region between 2 markers used in these studies. By family linkage studies using RFLPs, Sacchi et al. (1988) demonstrated that ERG is situated just proximal to ETS2. Mavrothalassitis et al. (1990) demonstrated that the ETS2 gene has no TATA box or CAAT box in its promoter. It has an alternative structure that serves a comparable function. The p16(INK4A) cyclin-dependent kinase inhibitor (CDKN2A; 600160) is implicated in replicative senescence, the state of permanent

growth arrest provoked by cumulative cell divisions or as a response to constitutive Ras–Raf–MEK signaling in somatic cells. Ohtani et al. (2001) demonstrated a role for the ETS1 and ETS2 transcription factors in regulating the expression of p16(INK4A) in these different contexts based on their ability to activate the p16(INK4A) promoter through an ETS binding site and their patterns of expression during the lifespan of human diploid fibroblasts. The induction of p16(INK4A) by ETS2, which is abundant in young human diploid fibroblasts, is potentiated by signaling through the Ras–Raf–MEK kinase cascade and inhibited by a direct interaction with the helix–loop–helix protein ID1 (OMIM Ref. No. 600349). In senescent cells, where the ETS2 levels and MEK signaling decline, the marked increase in p16(INK4A) expression is consistent with the reciprocal reduction of ID1 and accumulation of ETS1. Animal model experiments lend further support to the function of ETS2. Sumarsono et al. (1996) generated transgenic mice to investigate the consequences of overexpression of Ets2. They found that mice with less than 2-fold Ets2 overexpression in particular organs developed neurocranial, visceral cranial, and cervical skeletal abnormalities. These abnormalities had similarities with the

skeletal anomalies found in trisomy-16 mice and in humans with Down syndrome (OMIM Ref. No. 190685), in which the gene dosage of ETS2 is increased. The results were interpreted as indicating that ETS2 has a role in skeletal development and that overexpression is involved in the genesis of some skeletal abnormalities that occur in Down syndrome.

[66459] It is appreciated that the abovementioned animal model for ETS2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[66460] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66461] Le Beau, M. M.; Rowley, J. D.; Sacchi, N.; Watson, D. K.; Papas, T. S.; Diaz, M. O. : Hu-ets-2 is translocated to chromosome 8 in the t(8;21) in acute myelogenous leukemia. Cancer Genet. Cytogenet. 23: 269-274, 1986. ; and

[66462] Sumarsono, S. H.; Wilson, T. J.; Tymms, M. J.; Venter, D. J.; Corrick, C. M.; Kola, R.; Lahoud, M. H.; Papas, T. S.; Seth, A.; Kola, I. : Down's syndrome-like skeletal abnormalities in E.

[66463] Further studies establishing the function and utilities of

ETS2 are found in John Hopkins OMIM database record ID 164740, and in cited publications numbered 11230–11231, 11042, 1123 and 11233–11045 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Exostoses (multiple)–like 1 (EXTL1, Accession NM\_004455) is another VGAM1958 host target gene. EXTL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EXTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL1 BINDING SITE, designated SEQ ID:10756, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66464] Another function of VGAM1958 is therefore inhibition of Exostoses (multiple)–like 1 (EXTL1, Accession NM\_004455), a gene which probably contribute to the synthesis of heparan sulfate and heparin. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL1. The function of EXTL1 and its association with various diseases and clinical conditions, has been estab–

lished by previous studies, as described hereinabove with reference to VGAM806.Exostoses (multiple)-like 2 (EXTL2, Accession NM\_001439) is another VGAM1958 host target gene. EXTL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EXTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL2 BINDING SITE, designated SEQ ID:7162, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66465] Another function of VGAM1958 is therefore inhibition of Exostoses (multiple)-like 2 (EXTL2, Accession NM\_001439), a gene which is homologous to the EXT and EXTL genes. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL2. The function of EXTL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM743.Fanconi Anemia, Complementation Group F (FANCF, Accession NM\_022725) is another VGAM1958

host target gene. FANCF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FANCF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FANCF BINDING SITE, designated SEQ ID:22925, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66466] Another function of VGAM1958 is therefore inhibition of Fanconi Anemia, Complementation Group F (FANCF, Accession NM\_022725). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FANCF. Fibroblast Growth Factor 1 (acidic) (FGF1, Accession NM\_000800) is another VGAM1958 host target gene. FGF1 BINDING SITE1 through FGF1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGF1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF1 BINDING SITE1 through FGF1 BINDING SITE3, designated SEQ ID:6470, SEQ ID:26987 and SEQ

ID:26989 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66467] Another function of VGAM1958 is therefore inhibition of Fibroblast Growth Factor 1 (acidic) (FGF1, Accession NM\_000800), a gene which potent mitogen for a variety of cell types. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF1. The function of FGF1 has been established by previous studies. The endothelium, which consists of a single cell layer, protects blood vessels from thrombogenesis. Endothelial cell growth factor is a modifier of endothelial cell migration and proliferation and thus may be important in neovascularization. From a human brain stem cDNA library, Jaye et al. (1986) isolated 2 overlapping clones encoding ECGF. Southern blot analysis suggested that there is a single copy of the ECGF gene. In DNA from human-rodent hybrid cells, the probes showed 100% concordance with chromosome 5 and 98% concordance with HEXB (OMIM Ref. No. 606873), a chromosome 5 marker. The complete amino acid sequence was deduced from the nucleic acid sequence of these clones. The structure of the gene shows similarities to

that of interleukin-1 (OMIM Ref. No. 147720) with which it is about 30% homologous. To elucidate the structural determinants governing specificity in FGF signaling, Plotnikov et al. (2000) determined the crystal structures of FGF1 and FGF2 complexed with the immunoglobulin-like ligand-binding domains 2 and 3 (D2 and D3) of FGFR1 and FGFR2 (OMIM Ref. No. 176943), respectively. They found that highly conserved FGF-D2 and FGF-linker (between D2 and D3) interfaces define a general binding site for all FGF-FGFR complexes. Specificity is achieved through interactions between the N-terminal and central regions of FGFs and 2 loop regions in D3 that are subject to alternative splicing. These structures provide a molecular basis for FGF1 as a universal FGFR ligand and for modulation of FGF-FGFR specificity through primary sequence variations and alternative splicing. Pellegrini et al. (2000) reported the crystal structure of the FGFR2 ectodomain in a dimeric form that is induced by simultaneous binding to FGF1 and a heparin decasaccharide. The complex is assembled around a central heparin molecule linking 2 FGF1 ligands into a dimer that bridges between 2 receptor chains. The asymmetric heparin binding involves contacts with both FGF1 molecules but only 1 receptor chain. The



structure of the FGF1–FGFR2–heparin ternary complex provides a structural basis for the essential role of heparan sulfate in FGF signaling.

[66468] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66469] Plotnikov, A. N.; Hubbard, S. R.; Schlessinger, J.; Mohammadi, M. : Crystal structures of two FGF–FGFR complexes reveal the determinants of ligand–receptor specificity. *Cell* 101: 413–424, 2000. ; and

[66470] Pellegrini, L.; Burke, D. F.; von Delft, F.; Mulloy, B.; Blundell, T. L. : Crystal structure of fibroblast growth factor receptor ectodomain bound to ligand and heparin. *Nature* 407: 102.

[66471] Further studies establishing the function and utilities of FGF1 are found in John Hopkins OMIM database record ID 131220, and in cited publications numbered 11813–11817, 1166 and 11818–11821 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fragile X Mental Retardation 1 (FMR1, Accession NM\_002024) is another VGAM1958 host target gene. FMR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded

by FMR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FMR1 BINDING SITE, designated SEQ ID:7777, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66472] Another function of VGAM1958 is therefore inhibition of Fragile X Mental Retardation 1 (FMR1, Accession NM\_002024). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FMR1. FBJ Murine Osteosarcoma Viral Oncogene Homolog B (FOSB, Accession NM\_006732) is another VGAM1958 host target gene. FOSB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FOSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOSB BINDING SITE, designated SEQ ID:13581, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66473] Another function of VGAM1958 is therefore inhibition of

FBJ Murine Osteosarcoma Viral Oncogene Homolog B (FOSB, Accession NM\_006732), a gene which interacts with jun proteins enhancing their dna binding activity. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOSB. The function of FOSB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM747. Forkhead Box I1 (FOXI1, Accession NM\_012188) is another VGAM1958 host target gene. FOXI1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXI1 BINDING SITE, designated SEQ ID:14474, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66474] Another function of VGAM1958 is therefore inhibition of Forkhead Box I1 (FOXI1, Accession NM\_012188), a gene which plays an important role in the development of the cochlea and vestibulum, as well as embryogenesis. Ac-

cordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXI1. The function of FOXI1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1107. Thyroid Autoantigen 70kDa (Ku antigen) (G22P1, Accession NM\_001469) is another VGAM1958 host target gene. G22P1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by G22P1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G22P1 BINDING SITE, designated SEQ ID:7203, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66475] Another function of VGAM1958 is therefore inhibition of Thyroid Autoantigen 70kDa (Ku antigen) (G22P1, Accession NM\_001469), a gene which has a role in chromosome translocation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G22P1. The function of G22P1 and its association with various diseases and clinical

cal conditions, has been established by previous studies, as described hereinabove with reference to VGAM1052. Glucose-6-phosphatase, Catalytic (glycogen storage disease type I, von Gierke disease) (G6PC, Accession NM\_000151) is another VGAM1958 host target gene. G6PC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by G6PC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G6PC BINDING SITE, designated SEQ ID:5660, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66476] Another function of VGAM1958 is therefore inhibition of Glucose-6-phosphatase, Catalytic (glycogen storage disease type I, von Gierke disease) (G6PC, Accession NM\_000151). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G6PC. UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2) (GALNT2, Accession NM\_004481) is another VGAM1958 host target gene. GALNT2 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by GALNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT2 BINDING SITE, designated SEQ ID:10797, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66477] Another function of VGAM1958 is therefore inhibition of UDP-N-acetyl- $\alpha$ -D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2) (GALNT2, Accession NM\_004481), a gene which catalyzes the initial reaction in o-linked oligosaccharide biosynthesis. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT2. The function of GALNT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM187. Glycoprotein A Repeats Predominant (GARP, Accession NM\_005512) is another VGAM1958 host target gene. GARP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GARP, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GARP BINDING SITE, designated SEQ ID:12033, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66478] Another function of VGAM1958 is therefore inhibition of Glycoprotein A Repetitions Predominant (GARP, Accession NM\_005512). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GARP. GCN1 General Control of Amino-acid Synthesis 1-like 1 (yeast) (GCN1L1, Accession XM\_045792) is another VGAM1958 host target gene. GCN1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GCN1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCN1L1 BINDING SITE, designated SEQ ID:34568, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66479] Another function of VGAM1958 is therefore inhibition of

GCN1 General Control of Amino-acid Synthesis 1-like 1 (yeast) (GCN1L1, Accession XM\_045792), a gene which performs an EF3-related function on the ribosome by regulating GCN2 kinase activity. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCN1L1. The function of GCN1L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1438. Glucagon-like Peptide 1 Receptor (GLP1R, Accession NM\_002062) is another VGAM1958 host target gene. GLP1R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLP1R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLP1R BINDING SITE, designated SEQ ID:7828, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66480] Another function of VGAM1958 is therefore inhibition of Glucagon-like Peptide 1 Receptor (GLP1R, Accession NM\_002062), a gene which is mediated by g proteins



which activate adenylyl cyclase. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLP1R. The function of GLP1R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1652. Glutaminase (GLS, Accession NM\_014905) is another VGAM1958 host target gene. GLS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLS BINDING SITE, designated SEQ ID:17104, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66481] Another function of VGAM1958 is therefore inhibition of Glutaminase (GLS, Accession NM\_014905). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLS. Glutamate-ammonia Ligase (glutamine synthase) (GLUL, Accession NM\_002065) is another VGAM1958 host target gene. GLUL BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by GLUL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLUL BINDING SITE, designated SEQ ID:7836, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66482] Another function of VGAM1958 is therefore inhibition of Glutamate-ammonia Ligase (glutamine synthase) (GLUL, Accession NM\_002065), a gene which catalyzes the condensation of glutamate and ammonia to form glutamine. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLUL. The function of GLUL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM948. Glypican 1 (GPC1, Accession NM\_002081) is another VGAM1958 host target gene. GPC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of GPC1 BINDING SITE, designated SEQ ID:7868, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66483] Another function of VGAM1958 is therefore inhibition of Glypican 1 (GPC1, Accession NM\_002081), a gene which may play a role in growth control and differentiation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPC1. The function of GPC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. G Protein-coupled Receptor 61 (GPR61, Accession XM\_086232) is another VGAM1958 host target gene. GPR61 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR61, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR61 BINDING SITE, designated SEQ ID:38563, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4669.

[66484] Another function of VGAM1958 is therefore inhibition of G Protein-coupled Receptor 61 (GPR61, Accession XM\_086232), a gene which transduces extracellular signals through heterotrimeric G proteins. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR61. The function of GPR61 has been established by previous studies. By PCR of genomic DNA, Lee et al. (2001) obtained a partial GPR61 clone using primers designed from the sequence of a rabbit G protein-coupled receptor (GPCR). They used the PCR products to screen a human brain cDNA library and found that GPR61 encodes a 417-amino acid protein that shares over 80% identity with the rabbit homolog and 44% similarity with GPR62 (OMIM Ref. No. 606917) in the transmembrane region. By Northern blot analysis of human brain areas, Lee et al. (2001) detected a 4.3-kb transcript in caudate, putamen, and thalamus, but not in hypothalamus, hippocampus, pons, frontal cortex, or cerebellum. No expression was found in liver or kidney. Lee et al. (2001) also cloned rat GPR61 and, by in situ hybridization, found widespread expression in rat brain. Cikos et al. (2001) independently

cloned GPR61, which they called BALGR. A partial sequence was obtained by RT-PCR of human brain mRNA using degenerate oligonucleotides corresponding to a transmembrane sequence of GPR30 (OMIM Ref. No. 601805). They cloned the full-length cDNA from a hypothalamus cDNA library. They found that the deduced protein contains 451 amino acids and has a calculated molecular mass of about 49 kD. GPR61 contains 7 putative transmembrane domains, a potential N-glycosylation site, cysteine residues that may form a disulfide bridge, and several putative protein kinase sites. It also contains a conserved glu-arg-tyr sequence shared with other GPCRs. The highest sequence similarity (OMIM Ref. No. 28–31%) was found with biogenic amine GPCRs, i.e., serotonin, histamine, adrenergic, and dopamine GPCRs. By semiquantitative PCR of multiple human tissues, Cikos et al. (2001) found highest expression in brain and testes and low but detectable expression in all other tissues examined. Their results of Northern blot analysis of human brain regions differed from that reported by Lee et al. (2001). Strong expression of a 4.8-kb transcript was found in cerebral cortex, occipital pole, frontal lobe, temporal lobe, amygdala, and hippocampus, and lower expression in putamen

and caudate nucleus. No message was detected in cerebellum, medulla oblongata, spinal cord, corpus callosum, substantia nigra, subthalamic nucleus, or thalamus.

[66485] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66486] Cikos, S.; Gregor, P.; Koppel, J. : Cloning of a novel biogenic amine receptor-like G protein-coupled receptor expressed in human brain. *Biochim. Biophys. Acta* 1521: 66-72, 2001. ; and

[66487] Lee, D. K.; George, S. R.; Cheng, R.; Nguyen, T.; Liu, Y.; Brown, M.; Lynch, K. R.; O'Dowd, B. F. : Identification of four novel human G protein-coupled receptors expressed in the brain.

[66488] Further studies establishing the function and utilities of GPR61 are found in John Hopkins OMIM database record ID 606916, and in cited publications numbered 5504 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Growth Factor Receptor-bound Protein 10 (GRB10, Accession NM\_005311) is another VGAM1958 host target gene. GRB10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRB10, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRB10 BINDING SITE, designated SEQ ID:11786, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66489] Another function of VGAM1958 is therefore inhibition of Growth Factor Receptor-bound Protein 10 (GRB10, Accession NM\_005311), a gene which plays a functional role in insulin and IGF-I signaling. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRB10. The function of GRB10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM441. Guanine Nucleotide-releasing Factor 2 (specific for crk proto-oncogene) (GRF2, Accession NM\_005312) is another VGAM1958 host target gene. GRF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of GRF2 BINDING SITE, designated SEQ ID:11789, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66490] Another function of VGAM1958 is therefore inhibition of Guanine Nucleotide–releasing Factor 2 (specific for crk proto–oncogene) (GRF2, Accession NM\_005312), a gene which promotes the exchange of ras–bound gdp by gtp. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRF2. The function of GRF2 has been established by previous studies. C3G is a guanine nucleotide–releasing protein (GNRP) identified as a CRK (OMIM Ref. No. 164762) SH3–binding protein. Tanaka et al. (1994) suggested that the complex of C3G and CRK or C3G and GRB2/ASH (OMIM Ref. No. 108355) transduces signals from tyrosine kinases to RAS in a number of different tissues. Using fluorescence in situ hybridization, Takai et al. (1994) mapped the GRF2 gene to 9q34.3, where chromosomal changes have been reported in human hematopoietic malignancies.

[66491] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:



- [66492] Takai, S.; Tanaka, M.; Sugimura, H.; Yamada, K.; Naito, Y.; Kino, I.; Matsuda, M. : Mapping of the human C3G gene coding a guanine nucleotide releasing protein for Ras family to 9q34.3 by fluorescence in situ hybridization. Hum. Genet. 94: 549–550, 1994. ; and
- [66493] Tanaka, S.; Morishita, T.; Hashimoto, Y.; Hattori, S.; Nakamura, S.; Shibuya, M.; Matsuoka, K.; Takenawa, T.; Kurata, T.; Nagashima, K.; Matsuda, M. : C3G, a guanine nucleotide–releasin.
- [66494] Further studies establishing the function and utilities of GRF2 are found in John Hopkins OMIM database record ID 600303, and in cited publications numbered 1594–1595 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate Receptor, Metabotropic 7 (GRM7, Accession NM\_000844) is another VGAM1958 host target gene. GRM7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GRM7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM7 BINDING SITE, designated SEQ ID:6514, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA,

also designated SEQ ID:4669.

[66495] Another function of VGAM1958 is therefore inhibition of Glutamate Receptor, Metabotropic 7 (GRM7, Accession NM\_000844), a gene which is mediated by a g-protein that inhibits adenylate cyclase activity. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM7. The function of GRM7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM746. Guanylate Cyclase 1, Soluble, Beta 2 (GUCY1B2, Accession NM\_004129) is another VGAM1958 host target gene. GUCY1B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GUCY1B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GUCY1B2 BINDING SITE, designated SEQ ID:10334, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66496] Another function of VGAM1958 is therefore inhibition of Guanylate Cyclase 1, Soluble, Beta 2 (GUCY1B2, Accession

NM\_004129), a gene which is beta 2 subunit of soluble guanylate cyclase which converts GTP into the second messenger cGMP and plays a major role in the cardiovascular system as a receptor for nitric oxide. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GUCY1B2. The function of GUCY1B2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM379. Glycogen Synthase 1 (muscle) (GYS1, Accession XM\_114024) is another VGAM1958 host target gene. GYS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GYS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GYS1 BINDING SITE, designated SEQ ID:42624, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66497] Another function of VGAM1958 is therefore inhibition of Glycogen Synthase 1 (muscle) (GYS1, Accession XM\_114024), a gene which transfers the glycosyl residue

from udp-gluc to the nonreducing end of alpha-1,4-glucan. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GYS1. The function of GYS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1323.L-3-hydroxyacyl-Coenzyme A Dehydrogenase, Short Chain (HADHSC, Accession NM\_005327) is another VGAM1958 host target gene. HADHSC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HADHSC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HADHSC BINDING SITE, designated SEQ ID:11798, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66498] Another function of VGAM1958 is therefore inhibition of L-3-hydroxyacyl-Coenzyme A Dehydrogenase, Short Chain (HADHSC, Accession NM\_005327). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with HADHSC. Huntingtin-associated Protein 1 (neuroan 1) (HAP1, Accession NM\_003949) is another VGAM1958 host target gene. HAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HAP1 BINDING SITE, designated SEQ ID:10075, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66499] Another function of VGAM1958 is therefore inhibition of Huntingtin-associated Protein 1 (neuroan 1) (HAP1, Accession NM\_003949), a gene which functions as an adaptor protein using coiled coils to mediate interactions among cytoskeletal, vascular, and motor proteins. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HAP1. The function of HAP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM126. Holocytochrome C Synthase (cytochrome c heme-lyase) (HCCS, Accession

NM\_005333) is another VGAM1958 host target gene.

HCCS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HCCS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCCS BINDING SITE, designated SEQ ID:11806, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66500] Another function of VGAM1958 is therefore inhibition of Holocytochrome C Synthase (cytochrome c heme-lyase) (HCCS, Accession NM\_005333), a gene which catalyzes the covalent addition of a heme group onto c-type cytochromes in mitochondria. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCCS. The function of HCCS has been established by previous studies. Microphthalmia with linear skin defects syndrome (MLS; 309801) is an X-linked male-lethal disorder associated with X-chromosomal rearrangements resulting in monosomy from Xpter to Xp22. Features include microphthalmia, sclerocornea, linear skin defects, and agenesis of the corpus callosum. Using a cross-species con-

servation strategy, Schaefer et al. (1996) isolated an expressed sequence from the 450- to 550-kb MLS critical region on Xp22 by screening a human embryo cDNA library. Northern analysis demonstrated a transcript of approximately 2.6 kb in all tissues examined, with weaker expression of 1.2- and 5.2-kb transcripts. The strongest expression was observed in heart and skeletal muscle. Sequence analysis of a 3-kb cDNA contig revealed an 807-bp open reading frame encoding a putative 268-amino acid protein. Comparison of the sequence with sequences in databases revealed homology with holocytochrome c-type synthetases, which catalyze the covalent addition of a heme group onto c-type cytochromes in mitochondria. The c-type cytochromes are required for proper functioning of the electron transport pathway. The human gene, symbolized HCCS, and the corresponding murine gene characterized by Schaefer et al. (1996) share 83% nucleotide sequence identity and 85% amino acid identity. The authors stated that, because of the lack of a neuromuscular phenotype in MLS, it is uncertain how the deletion of a mitochondrial holocytochrome synthetase would contribute to phenotype seen in MLS. The expression pattern of the gene and knowledge of the function of

holocytochrome synthetases suggested, however, that it is a good candidate for X-linked encephalomyopathies typically associated with mitochondrial dysfunction. Based on its chromosomal location and its role in the mitochondrial respiratory chain, HCCS was considered a candidate gene for Rett syndrome (RTT; 312750). The genomic structure of the gene, which occupies an 11-kb region and consists of 7 exons, was determined. No mutational abnormality of the gene was found in 20 RTT patients (Van den Veyver et al., 1998).

- [66501] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [66502] Schaefer, L.; Ballabio, A.; Zoghbi, H. Y. : Cloning and characterization of a putative human holocytochrome c-type synthetase gene (HCCS) isolated from the critical region for microphthalmia with linear skin defects (MLS). *Genomics* 34: 166–172, 1996. ; and
- [66503] Van den Veyver, I. B.; Subramanian, S.; Zoghbi, H. Y. : Genomic structure of a human holocytochrome c-type synthetase gene in Xp22.3 and mutation analysis in patients with Rett syndrome.
- [66504] Further studies establishing the function and utilities of



HCCS are found in John Hopkins OMIM database record ID 300056, and in cited publications numbered 9005–9006 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Histone Deacetylase 5 (HDAC5, Accession NM\_139205) is another VGAM1958 host target gene. HDAC5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HDAC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC5 BINDING SITE, designated SEQ ID:29223, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66505] Another function of VGAM1958 is therefore inhibition of Histone Deacetylase 5 (HDAC5, Accession NM\_139205), a gene which is responsible for the deacetylation of lysine residues on the n-terminal part of the core histones and mediate transcriptional regulation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC5. The function of HDAC5 and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM263.Hepatoma-derived Growth Factor (high-mobility group protein 1-like) (HDGF, Accession NM\_004494) is another VGAM1958 host target gene. HDGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HDGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDGF BINDING SITE, designated SEQ ID:10830, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66506] Another function of VGAM1958 is therefore inhibition of Hepatoma-derived Growth Factor (high-mobility group protein 1-like) (HDGF, Accession NM\_004494), a gene which is a heparin-binding protein, with mitogenic activity for fibroblasts. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDGF. The function of HDGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1929.Homeo Box B7 (HOXB7, Accession

NM\_004502) is another VGAM1958 host target gene. HOXB7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXB7 BINDING SITE, designated SEQ ID:10837, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66507] Another function of VGAM1958 is therefore inhibition of Homeo Box B7 (HOXB7, Accession NM\_004502), a gene which is a member of homeodomain family of DNA binding proteins; may regulate gene expression, morphogenesis, and differentiation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXB7. The function of HOXB7 has been established by previous studies. In mouse, Hoxb7 expression is confined to macrophages. Using RT-PCR, Lill et al. (1995) detected expression of HOXB7 in monocytes differentiated from HL60 cells by stimulation with vitamin D3. Overexpression of HOXB7 inhibited differentiation into granulocytes but

not monocytes. However, RT-PCR analysis failed to detect HOXB7 expression in mature monocytes. HOX proteins have a conserved DNA-binding homeodomain, a pentapeptide motif that mediates interactions with PBX proteins (e.g., PBX1; 176310), and an N-terminal octapeptide motif. Yaron et al. (2001) found that wildtype HOXB7 inhibited differentiation of a murine myelomonocytic cell line, 32D, but that mutations in any of the conserved regions blocked this inhibitory effect. Mutations in casein kinase phosphorylation sites, the glutamate-rich C terminus, or the N-terminal 14 residues of HOXB7 enhanced 32D differentiation.

[66508] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66509] Lill, M. C.; Fuller, J. F.; Herzig, R.; Crooks, G. M.; Gasson, J. C. : The role of the homeobox gene, HOX B7, in human myelomonocytic differentiation. Blood 85: 692-697, 1995. ; and

[66510] Yaron, Y.; McAdara, J. K.; Lynch, M.; Hughes, E.; Gasson, J. C. : Identification of novel functional regions important for the activity of HOXB7 in mammalian cells. J. Immun. 166: 5058-5.

[66511] Further studies establishing the function and utilities of HOXB7 are found in John Hopkins OMIM database record ID 142962, and in cited publications numbered 5207–2659 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Homeo Box C5 (HOXC5, Accession NM\_018953) is another VGAM1958 host target gene. HOXC5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HOXC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXC5 BINDING SITE, designated SEQ ID:21021, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66512] Another function of VGAM1958 is therefore inhibition of Homeo Box C5 (HOXC5, Accession NM\_018953). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXC5. 5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868) is another VGAM1958 host target gene. HTR2C BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by HTR2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR2C BINDING SITE, designated SEQ ID:6531, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66513] Another function of VGAM1958 is therefore inhibition of 5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM\_000868), a gene which activates phospholipase C and regulates intracellular calcium flux. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR2C. The function of HTR2C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1052. Islet Cell Autoantigen 1, 69kDa (ICA1, Accession NM\_022308) is another VGAM1958 host target gene. ICA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of ICA1 BINDING SITE, designated SEQ ID:22738, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66514] Another function of VGAM1958 is therefore inhibition of Islet Cell Autoantigen 1, 69kDa (ICA1, Accession NM\_022308), a gene which Islet cell autoantigen 1. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICA1. The function of ICA1 has been established by previous studies. Pietropaolo et al. (1993) identified a novel 69-kD peptide autoantigen (ICA69) associated with insulin-dependent diabetes mellitus (IDDM) by screening a human islet lambda-gt11 cDNA expression library with cytoplasmic islet cell antibody positive sera from relatives of IDDM patients who progressed to the overt disease. The deduced open reading frame of the ICA69 cDNA predicted a 483-amino acid protein. ICA69 showed no nucleotide or amino acid sequence relation to any known sequence in GenBank except for 2 short regions of similarity with bovine serum albumin (BSA). The ICA69 cDNA probe hybridized with a 2-kb mRNA in polyadenylated RNA from human pancreas, brain, heart,

thyroid, and kidney. The structural gene for ICA69 was designated ICA1. A homolog in the mouse, designated *Ica1*, was mapped to the proximal end of chromosome 6, within 6 cM of the MET protooncogene (OMIM Ref. No. 164860). One can deduce from homology of synteny that the human ICA1 gene is probably located in the region 7q31, which is conserved between mouse and human. Thus, Pietropaolo et al. (1993) added another islet antigen to the isoforms of the neuroendocrine-associated enzyme glutamic acid decarboxylase (GAD; 138275) which react with sera from IDDM patients as well as from patients with stiff-man syndrome (OMIM Ref. No. 184850). However, by isotopic in situ hybridization, Gaedigk et al. (1994) demonstrated that the ICA1 gene maps to human 7p22. Gaedigk et al. (1996) reported that the mouse *Ica1* gene is distributed over more than 100 kb on chromosome 6. The single murine genomic locus contains 14 coding exons, ranging from 39 to 271 bp in length. They found that the human and mouse intron/exon junctions are identical. They cloned cDNAs and identified alternatively spliced mRNA transcripts. All splice variants encoded the conserved T-cell epitope (in exon 2) recognized by autoreactive T cells in diabetic children and diabetes-prone NOD



mice.

[66515] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66516] Gaedigk, R.; Duncan, A. M. V.; Miyazaki, I.; Robinson, B. H.; Dosch, H.-M. : ICA1 encoding p69, a protein linked to the development of type 1 diabetes, maps to human chromosome 7p22. Cytogenet. Cell Genet. 66: 274-276, 1994. ; and

[66517] Gaedigk, R.; Karges, W.; Hui, M. F.; Scherer, S. W.; Dosch, H.-M. : Genomic organization and transcript analysis of ICAp69, a target antigen in diabetic autoimmunity. Genomics 38: 382-39.

[66518] Further studies establishing the function and utilities of ICA1 are found in John Hopkins OMIM database record ID 147625, and in cited publications numbered 11408-11410 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Inducible T-cell Co-stimulator (ICOS, Accession NM\_012092) is another VGAM1958 host target gene. ICOS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICOS, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICOS BINDING SITE, designated SEQ ID:14385, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66519] Another function of VGAM1958 is therefore inhibition of Inducible T-cell Co-stimulator (ICOS, Accession NM\_012092), a gene which forms homodimers and functions as an inducible T-cell co-stimulator. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICOS. The function of ICOS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18. Isocitrate Dehydrogenase 3 (NAD<sup>+</sup>) Alpha (IDH3A, Accession NM\_005530) is another VGAM1958 host target gene. IDH3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IDH3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IDH3A BINDING SITE, designated SEQ ID:12052, to the nucleotide sequence of

VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66520] Another function of VGAM1958 is therefore inhibition of Isocitrate Dehydrogenase 3 (NAD<sup>+</sup>) Alpha (IDH3A, Accession NM\_005530), a gene which decarboxylates isocitrate into alpha-ketoglutarate in the TCA cycle. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IDH3A. The function of IDH3A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM349. Interferon (alpha, beta and omega) Receptor 1 (IFNAR1, Accession NM\_000629) is another VGAM1958 host target gene. IFNAR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IFNAR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IFNAR1 BINDING SITE, designated SEQ ID:6246, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66521] Another function of VGAM1958 is therefore inhibition of

Interferon (alpha, beta and omega) Receptor 1 (IFNAR1, Accession NM\_000629), a gene which is a receptor for interferons alpha and beta. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IFNAR1. The function of IFNAR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM904. Interleukin 1 Receptor, Type I (IL1R1, Accession NM\_000877) is another VGAM1958 host target gene. IL1R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1R1 BINDING SITE, designated SEQ ID:6562, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66522] Another function of VGAM1958 is therefore inhibition of Interleukin 1 Receptor, Type I (IL1R1, Accession NM\_000877), a gene which is a receptor for interleukin-1 alpha (il-1a), beta (il-1b), and interleukin-1 receptor antagonist protein (il-1ra). Accordingly, utilities of

VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1R1. The function of IL1R1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM704. Inhibin, Beta C (INHBC, Accession NM\_005538) is another VGAM1958 host target gene. INHBC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INHBC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INHBC BINDING SITE, designated SEQ ID:12063, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66523] Another function of VGAM1958 is therefore inhibition of Inhibin, Beta C (INHBC, Accession NM\_005538), a gene which inhibits the secretion of follitropin by the pituitary gland. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INHBC. The function of INHBC and its association with various diseases and clinical condi-

tions, has been established by previous studies, as described hereinabove with reference to VGAM89. Interleukin-1 Receptor-associated Kinase 4 (IRAK4, Accession XM\_028349) is another VGAM1958 host target gene. IRAK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRAK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRAK4 BINDING SITE, designated SEQ ID:30694, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66524] Another function of VGAM1958 is therefore inhibition of Interleukin-1 Receptor-associated Kinase 4 (IRAK4, Accession XM\_028349), a gene which may function as an IRAK1 kinase, triggering a cascade of phosphorylation events. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRAK4. The function of IRAK4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1291. Integrin,

Alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor) (ITGA2, Accession NM\_002203) is another VGAM1958 host target gene. ITGA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA2 BINDING SITE, designated SEQ ID:7961, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66525] Another function of VGAM1958 is therefore inhibition of Integrin, Alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor) (ITGA2, Accession NM\_002203), a gene which has roles in blood clotting and angiogenesis, acts as a collagen and laminin receptor. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA2. The function of ITGA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827. Integrin, Alpha 6 (ITGA6, Accession NM\_000210) is another VGAM1958 host target gene.

ITGA6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA6 BINDING SITE, designated SEQ ID:5701, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66526] Another function of VGAM1958 is therefore inhibition of Integrin, Alpha 6 (ITGA6, Accession NM\_000210). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA6. JJAZ1 (Accession NM\_015355) is another VGAM1958 host target gene. JJAZ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JJAZ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JJAZ1 BINDING SITE, designated SEQ ID:17655, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66527] Another function of VGAM1958 is therefore inhibition of



JJAZ1 (Accession NM\_015355), a gene which is a zinc finger protein. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JJAZ1. The function of JJAZ1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM231. Jumonji Homolog (mouse) (JMJ, Accession NM\_004973) is another VGAM1958 host target gene. JMJ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JMJ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JMJ BINDING SITE, designated SEQ ID:11419, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66528] Another function of VGAM1958 is therefore inhibition of Jumonji Homolog (mouse) (JMJ, Accession NM\_004973), a gene which participates in the negative regulation of cell growth. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JMJ. The function of JMJ and its

association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM523. Jerky Homolog (mouse) (JRK, Accession XM\_098818) is another VGAM1958 host target gene. JRK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JRK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JRK BINDING SITE, designated SEQ ID:41837, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66529] Another function of VGAM1958 is therefore inhibition of Jerky Homolog (mouse) (JRK, Accession XM\_098818), a gene which might function as a DNA-binding protein. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JRK. The function of JRK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM210. Potassium Voltage-gated Channel, Shaker-related Subfamily, Beta Member 1

(KCNAB1, Accession XM\_027634) is another VGAM1958 host target gene. KCNAB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNAB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNAB1 BINDING SITE, designated SEQ ID:30545, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66530] Another function of VGAM1958 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Beta Member 1 (KCNAB1, Accession XM\_027634), a gene which is the regulatory beta subunit for a shaker-related voltage-gated potassium channel. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNAB1. The function of KCNAB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM727. Potassium Inwardly-rectifying Channel, Subfamily J, Member 16 (KCNJ16, Accession NM\_018658) is another VGAM1958 host target gene.

KCNJ16 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KCNJ16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ16 BINDING SITE, designated SEQ ID:20726, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66531] Another function of VGAM1958 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 16 (KCNJ16, Accession NM\_018658). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ16. Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 3 (KCNS3, Accession NM\_002252) is another VGAM1958 host target gene. KCNS3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KCNS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNS3 BINDING SITE, designated SEQ

ID:8049, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66532] Another function of VGAM1958 is therefore inhibition of Potassium Voltage-gated Channel, Delayed-rectifier, Sub-family S, Member 3 (KCNS3, Accession NM\_002252). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNS3. Ketohexokinase (fructokinase) (KHK, Accession NM\_006488) is another VGAM1958 host target gene. KHK BINDING SITE1 and KHK BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KHK, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KHK BINDING SITE1 and KHK BINDING SITE2, designated SEQ ID:13214 and SEQ ID:5729 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66533] Another function of VGAM1958 is therefore inhibition of Ketohexokinase (fructokinase) (KHK, Accession NM\_006488). Accordingly, utilities of VGAM1958 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with KHK. Kinesin Family Member 5C (KIF5C, Accession NM\_004522) is another VGAM1958 host target gene. KIF5C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF5C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF5C BINDING SITE, designated SEQ ID:10853, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66534] Another function of VGAM1958 is therefore inhibition of Kinesin Family Member 5C (KIF5C, Accession NM\_004522). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF5C. Kinesin-like 3 (KNSL3, Accession NM\_005355) is another VGAM1958 host target gene. KNSL3 BINDING SITE1 and KNSL3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KNSL3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of KNSL3 BINDING SITE1 and KNSL3 BINDING SITE2, designated SEQ ID:11824 and SEQ ID:24962 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66535] Another function of VGAM1958 is therefore inhibition of Kinesin-like 3 (KNSL3, Accession NM\_005355), a gene which may function in intracellular transport and mitosis. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KNSL3. The function of KNSL3 has been established by previous studies. Janatipour et al. (1992) identified the HSET gene within a segment centromeric to the class II gene region of the human major histocompatibility complex. By screening a human testis library with a cDNA corresponding to Tctex7, the mouse homolog of HSET, Ando et al. (1994) isolated human HSET cDNAs. Northern blot analysis revealed that the 2.4-kb HSET mRNA is expressed in several human cell lines. The C-terminal 350 amino acids of the predicted HSET protein share extensive homology with the ATP-binding and motor domains of kinesin heavy chain (OMIM Ref. No. 148760) and the kinesin-related proteins CENPE (OMIM

Ref. No. 117143) and MKLP1. Although the mechanochemical domain of kinesin and kinesin-like proteins is generally located within the N-terminal region, HSET contains a C-terminal mechanochemical domain. This 'reversed' structural organization is also found in the *S. cerevisiae* KAR3 and *Drosophila* Ncd kinesin-like proteins. Molecular motors move directionally to either the plus or the minus ends of microtubules or actin filaments. For example, kinesin (see OMIM Ref. No. 600025) moves towards the plus end, whereas the *Drosophila* Ncd motor moves towards the minus end. Endow and Higuchi (2000) showed that an asn340-to-lys mutation in the 'neck' (the region between the stalk and the C-terminal motor domain) of Ncd, which corresponds to a KAR3 mutation obtained in a yeast suppressor screen (Hoyt et al., 1993), causes the motor to abruptly reverse directions and move toward either the plus or minus end. Velocity in mutant and wildtype was identical, indicating that the neck was functional. Mutation of lys640, which is located in the motor-core region and touches asn340 in crystal structures, to asn caused the same phenotype. Analysis of a double mutant for these residues, which did not revert to minus-end directionality, indicated that the highly con-



served residues do not interact normally in an inverted configuration. Endow and Higuchi (2000) concluded that directional bias is dependent on neck/motor-core interactions.

[66536] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66537] Janatipour, M.; Naumov, Y.; Ando, A.; Sugimura, K.; Okamoto, N.; Tsuji, K.; Abe, K.; Inoko, H. : Search for MHC-associated genes in human: five new genes centromeric to HLA-DP with yet unknown functions. Immunogenetics 35: 272-278, 1992. ; and

[66538] Janitz, K.; Wild, A.; Beck, S.; Savasta, S.; Beluffi, G.; Ziegler, A.; Volz, A. : Genomic organization of the HSET locus and the possible association of HLA-linked genes with immotile ci.

[66539] Further studies establishing the function and utilities of KNSL3 are found in John Hopkins OMIM database record ID 603815, and in cited publications numbered 491 and 12002 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LANGERIN (Accession NM\_015717) is another VGAM1958 host target gene. LANGERIN BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LANGERIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LANGERIN BINDING SITE, designated SEQ ID:17931, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66540] Another function of VGAM1958 is therefore inhibition of LANGERIN (Accession NM\_015717), a gene which could be involved in endocytosis. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LANGERIN. The function of LANGERIN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM688. Low Density Lipoprotein Receptor (familial hypercholesterolemia) (LDLR, Accession NM\_000527) is another VGAM1958 host target gene. LDLR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LDLR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of LDLR BINDING SITE, designated SEQ ID:6128, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66541] Another function of VGAM1958 is therefore inhibition of Low Density Lipoprotein Receptor (familial hypercholesterolemia) (LDLR, Accession NM\_000527), a gene which also acts as a tumor suppressor. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDLR. The function of LDLR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1030. LENG4 (Accession NM\_024298) is another VGAM1958 host target gene. LENG4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LENG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LENG4 BINDING SITE, designated SEQ ID:23584, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66542] Another function of VGAM1958 is therefore inhibition of LENG4 (Accession NM\_024298), a gene which may be a transmembrane protein. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LENG4. The function of LENG4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259. LNK (Accession NM\_005475) is another VGAM1958 host target gene. LNK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LNK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LNK BINDING SITE, designated SEQ ID:11974, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66543] Another function of VGAM1958 is therefore inhibition of LNK (Accession NM\_005475), a gene which links T-cell receptor activation signal to phospholipase c-gamma-1, grb-2 and phosphatidylinositol 3-kinase (by similarity). Accordingly, utilities of VGAM1958 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with LNK. The function of LNK and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM115. Lipoprotein Lipase (LPL, Accession NM\_000237) is another VGAM1958 host target gene. LPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPL BINDING SITE, designated SEQ ID:5749, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66544] Another function of VGAM1958 is therefore inhibition of Lipoprotein Lipase (LPL, Accession NM\_000237), a gene which is the hydrolysis of triglycerides of circulating chylomicrons and very low density lipoproteins (vldl). the enzyme functions in the presence of apolipoprotein c-2 on the luminal surface of vascular. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPL. The function of LPL and its association with various dis-

eases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Lecithin Retinol Acyltransferase (phosphatidylcholine--retinol O-acyltransferase) (LRAT, Accession XM\_011181) is another VGAM1958 host target gene. LRAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRAT BINDING SITE, designated SEQ ID:30180, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66545] Another function of VGAM1958 is therefore inhibition of Lecithin Retinol Acyltransferase (phosphatidylcholine--retinol O-acyltransferase) (LRAT, Accession XM\_011181). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRAT. Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM\_035037) is another VGAM1958 host target gene. LRP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

LRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP4 BINDING SITE, designated SEQ ID:32202, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66546] Another function of VGAM1958 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM\_035037). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP4. Leucine-zipper-like Transcriptional Regulator, 1 (LZTR1, Accession NM\_006767) is another VGAM1958 host target gene. LZTR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LZTR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTR1 BINDING SITE, designated SEQ ID:13637, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66547] Another function of VGAM1958 is therefore inhibition of

Leucine–zipper–like Transcriptional Regulator, 1 (LZTR1, Accession NM\_006767). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTR1. V–maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog F (avian) (MAFF, Accession NM\_012323) is another VGAM1958 host target gene. MAFF BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAFF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAFF BINDING SITE, designated SEQ ID:14701, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66548] Another function of VGAM1958 is therefore inhibition of V–maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog F (avian) (MAFF, Accession NM\_012323), a gene which Binds to the US–2 motif of the oxytocin receptor gene; has a leucine zipper structure. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAFF. The function of MAFF and its association with vari–



ous diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1928. Mannosidase, Alpha, Class 2A, Member 2 (MAN2A2, Accession NM\_006122) is another VGAM1958 host target gene. MAN2A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAN2A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN2A2 BINDING SITE, designated SEQ ID:12766, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66549] Another function of VGAM1958 is therefore inhibition of Mannosidase, Alpha, Class 2A, Member 2 (MAN2A2, Accession NM\_006122), a gene which is an enzyme involved in the processing of N-linked glycans. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN2A2. The function of MAN2A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM1794.Microtubule-associated Protein 2 (MAP2, Accession NM\_031846) is another VGAM1958 host target gene. MAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2 BINDING SITE, designated SEQ ID:25581, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66550] Another function of VGAM1958 is therefore inhibition of Microtubule-associated Protein 2 (MAP2, Accession NM\_031846), a gene which may act in stabilizing microtubules against depolymerization.also seems to have a stiffening effect on microtubules. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2. The function of MAP2 has been established by previous studies. For nerve cells to develop their highly polarized form, appropriate structural molecules must be targeted to either axons or dendrites. This could be achieved by the synthesis of structural proteins in the cell body and their sorting to either axons or dendrites by specific

transport mechanisms. For dendrites, an alternative possibility is that proteins could be synthesized locally in the dendritic cytoplasm. This would allow regulation of the production of structural molecules in response to local demand during dendritic development. The existence of dendritic polyribosomes and the demonstration that newly synthesized RNA is transported into the dendrites of neurons differentiating in culture support the feasibility of dendritic protein synthesis. By in situ hybridization with specific cDNA probes, Garner et al. (1988) showed that mRNA for the dendrite-specific microtubule-associated protein MAP2 was present in dendrites in the developing brain. By contrast, the mRNA for tubulin (OMIM Ref. No. 191120), a protein present in both axons and dendrites, was localized exclusively in neuronal cell bodies. Animal model experiments lend further support to the function of MAP2. Marsden et al. (1996) produced transgenic mice that overexpress embryonic Map2 (referred to by them as MAP2c) without inducing detectable effects on the morphology of neurons. The transgenic MAP2c was present in dendrites but not in axons but transgenic MAP2c messenger RNA was limited to cell bodies. The authors concluded that dendritic localization of transgenic MAP2c protein

was not the result of previous transport of its mRNA but implies the existence of a protein-based mechanism capable of sorting MAP2 protein isoforms

[66551] It is appreciated that the abovementioned animal model for MAP2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[66552] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66553] Garner, C. C.; Tucker, R. P.; Matus, A. : Selective localization of messenger RNA for cytoskeletal protein MAP2 in dendrites. *Nature* 336: 674–677, 1988. ; and

[66554] Marsden, K. M.; Doll, T.; Ferralli, J.; Botteri, F.; Matus, A. : Transgenic expression of embryonic MAP2 in adult mouse brain: implications for neuronal polarization. *J. Neurosci.* 16: 3265–.

[66555] Further studies establishing the function and utilities of MAP2 are found in John Hopkins OMIM database record ID 157130, and in sited publications numbered 10752–10756 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mitogen-activated Protein Kinase Kinase 2 (MAP2K2,

Accession NM\_030662) is another VGAM1958 host target gene. MAP2K2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAP2K2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K2 BINDING SITE, designated SEQ ID:24995, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66556] Another function of VGAM1958 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 2 (MAP2K2, Accession NM\_030662), a gene which is a signaling intermediate, activates ERK1. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K2. The function of MAP2K2 has been established by previous studies. See MEK1 (OMIM Ref. No. 176872). Zheng and Guan (1993) isolated and sequenced 2 human cDNAs encoding members of the MAP kinase kinase (MAP2K) family, designated MEK1 and MEK2 by them. The MEK2 cDNA encodes a predicted 400-amino acid protein that shares 80% sequence identity with human MEK1. Zheng and Guan

(1993) showed that recombinant MEK2 and MEK1 both could activate human ERK1 (OMIM Ref. No. 601795) in vitro. They further characterized biochemically the 2 MAP2Ks. Influenza A viruses are significant causes of morbidity and mortality worldwide. Annually updated vaccines may prevent disease, and antivirals are effective treatment early in disease when symptoms are often non-specific. Viral replication is supported by intracellular signaling events. Using U0126, a nontoxic inhibitor of MEK1 and MEK2, and thus an inhibitor of the RAF1 (OMIM Ref. No. 164760)/MEK/ERK pathway (see OMIM Ref. No. Favata et al. (1998)), Pleschka et al. (2001) examined the cellular response to infection with influenza A. U0126 suppressed both the early and late ERK activation phases after virus infection. Inhibition of the signaling pathway occurred without impairing the synthesis of viral RNA or protein, or the import of viral ribonucleoprotein complexes (RNP) into the nucleus. Instead, U0126 inhibited RAF/MEK/ERK signaling and the export of viral RNP without affecting the cellular mRNA export pathway. Pleschka et al. (2001) proposed that ERK regulates a cellular factor involved in the viral nuclear export protein function. They suggested that local application of MEK inhibitors may have only minor

toxic effects on the host while inhibiting viral replication without giving rise to drug-resistant virus variants

[66557] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66558] Zheng, C. F.; Guan, K. L. : Cloning and characterization of two distinct human extracellular signal-regulated kinase activator kinases, MEK1 and MEK2. J. Biol. Chem. 268: 11435–11439, 1993. ; and

[66559] Pleschka, S.; Wolff, T.; Ehrhardt, C.; Hobom, G.; Planz, O.; Rapp, U. R.; Ludwig, S. : Influenza virus propagation is impaired by inhibition of the Raf/MEK/ERK signalling cascade. Nature Ce.

[66560] Further studies establishing the function and utilities of MAP2K2 are found in John Hopkins OMIM database record ID 601263, and in cited publications numbered 10344, 10346–10348, 1035 and 10356 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mitogen-activated Protein Kinase 1 (MAPK1, Accession NM\_138957) is another VGAM1958 host target gene. MAPK1 BINDING SITE1 and MAPK1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPK1, corresponding to

HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK1 BINDING SITE1 and MAPK1 BINDING SITE2, designated SEQ ID:29063 and SEQ ID:8616 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66561] Another function of VGAM1958 is therefore inhibition of Mitogen-activated Protein Kinase 1 (MAPK1, Accession NM\_138957), a gene which phosphorylates microtubule-associated protein-2 (map2). myelin basic protein (mbp), and elk-1; may promote entry in the cell cycle. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK1. The function of MAPK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. Mitogen-activated Protein Kinase 9 (MAPK9, Accession NM\_139068) is another VGAM1958 host target gene. MAPK9 BINDING SITE1 through MAPK9 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPK9, corresponding to HOST TARGET binding sites



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK9 BINDING SITE1 through MAPK9 BINDING SITE4, designated SEQ ID:29135, SEQ ID:29137, SEQ ID:29139 and SEQ ID:8630 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66562] Another function of VGAM1958 is therefore inhibition of Mitogen-activated Protein Kinase 9 (MAPK9, Accession NM\_139068), a gene which Member of the MAP kinase family, regulates c-Jun in response to proinflammatory cytokines and UV irradiation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK9. The function of MAPK9 has been established by previous studies. The transcriptional activity of the c-Jun protooncoprotein (see OMIM Ref. No. 165160) is augmented through phosphorylation at 2 sites by c-Jun amino-terminal kinases (JNKs). Using in-gel kinase assays, Hibi et al. (1993) identified 2 JNKs, 46 and 55 kD in size. The 46-kD protein JNK1 (OMIM Ref. No. 601158) was shown to be a member of the mitogen-activated protein kinase (MAPK) family. Using a JNK1 cDNA as a probe, Kallunki et

al. (1994) and Sluss et al. (1994) isolated cDNAs encoding the 55-kD protein, which both designated JNK2. Kallunki et al. (1994) reported that the sequence of the predicted 424-amino acid JNK2 protein is 83% identical to that of JNK1. Both JNKs contain a Thr-Pro-Tyr phosphorylation motif. Expression of JNK2 in mammalian cells potentiated activation of a c-Jun-responsive promoter, while expression of JNK1 had no effect. Using in vitro binding assays, Kallunki et al. (1994) found that JNK2 bound c-Jun approximately 25 times more efficiently than did JNK1. The authors traced this difference to a small beta-strand-like region near the catalytic pocket of the enzyme. Northern blot analysis revealed that JNK2 is expressed as multiple transcripts in many cell types. Sluss et al. (1994) demonstrated that both UV radiation and the proinflammatory cytokine TNF- $\alpha$  (OMIM Ref. No. 191160) induce JNK1 and JNK2. Animal model experiments lend further support to the function of MAPK9. Tournier et al. (2000) demonstrated that JNK is required for UV-induced apoptosis in primary murine embryonic fibroblasts. Fibroblasts with simultaneous targeted disruptions of JNK1 and JNK2 genes were protected against UV-stimulated apoptosis. The absence of JNK caused a defect in the mitochondrial death

signaling pathway, including the failure to release cytochrome c. These data indicated that mitochondria are influenced by proapoptotic signal transduction through the JNK pathway. Dong et al. (2000) used 3 new mouse models in which peripheral T cells completely lack JNK proteins or signaling to test whether the JNK signaling pathway is crucial for IL2 expression and T-cell activation. Unexpectedly, these T cells made more IL2 (OMIM Ref. No. 147680) and proliferated better than wildtype cells. However, production of effector T-cell cytokines did require JNK. Thus, Dong et al. (2000) concluded that JNK is necessary for T-cell differentiation but not for naive T-cell activation

[66563] It is appreciated that the abovementioned animal model for MAPK9 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[66564] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66565] Dong, C.; Yang, D. D.; Tournier, C.; Whitmarsh, A. J.; Xu, J.; Davis, R. J.; Flavell, R. A. : JNK is required for effector T-cell function but not for T-cell activation. Nature 405:

91–94, 2000. ; and

[66566] Kallunki, T.; Su, B.; Tsigelny, I.; Sluss, H. K.; Derijard, B.; Moore, G.; Davis, R.; Karin, M. : JNK2 contains a specificity–determining region responsible for efficient c–Jun binding and.

[66567] Further studies establishing the function and utilities of MAPK9 are found in John Hopkins OMIM database record ID 602896, and in cited publications numbered 9463, 9464–590 and 9465 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Microtubule–associated Protein Tau (MAPT, Accession NM\_005910) is another VGAM1958 host target gene. MAPT BINDING SITE1 through MAPT BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPT, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPT BINDING SITE1 through MAPT BINDING SITE4, designated SEQ ID:12541, SEQ ID:18829, SEQ ID:18835 and SEQ ID:18841 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66568] Another function of VGAM1958 is therefore inhibition of Microtubule-associated Protein Tau (MAPT, Accession NM\_005910), a gene which Microtubule-associated protein tau; promotes microtubule assembly. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPT. The function of MAPT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. MAX Protein (MAX, Accession NM\_145112) is another VGAM1958 host target gene. MAX BINDING SITE1 and MAX BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAX, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAX BINDING SITE1 and MAX BINDING SITE2, designated SEQ ID:29716 and SEQ ID:8199 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66569] Another function of VGAM1958 is therefore inhibition of MAX Protein (MAX, Accession NM\_145112), a gene which

interacts specifically with the MYC (190080) protein . Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAX. The function of MAX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1923. MCM2 Minichromosome Maintenance Deficient 2, Mitotin (*S. cerevisiae*) (MCM2, Accession XM\_042618) is another VGAM1958 host target gene. MCM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MCM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCM2 BINDING SITE, designated SEQ ID:33721, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66570] Another function of VGAM1958 is therefore inhibition of MCM2 Minichromosome Maintenance Deficient 2, Mitotin (*S. cerevisiae*) (MCM2, Accession XM\_042618), a gene which Minichromosome maintenance protein; binds chromatin and regulates entry into S phase. Accordingly, utili-

ties of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCM2. The function of MCM2 has been established by previous studies. The replication of DNA occurs only once per cell cycle in eukaryotes. Blow and Laskey (1988) attempted to explain this tight control by proposing the existence of a hypothetical licensing factor that would bind to chromatin during mitosis to permit DNA replication during the ensuing S phase in *Xenopus* egg extracts. Kubota et al. (1995), Chong et al. (1995), and Madine et al. (1995) identified a replication licensing activity in a complex containing MCM/P1 family proteins in *Xenopus* oocytes. Burkhart et al. (1995) showed that human MCM2 and MCM5 (OMIM Ref. No. 602696) proteins form a complex. Hu et al. (1993) reported cDNA sequences for 5 MCM/P1 family members. MCM2, also called CDCL1 and BM28, is a human nuclear protein that may play an important role in 2 crucial steps of the cell cycle, namely, onset of DNA replication and cell division. It is similar to members of the family of early S-phase proteins. Using plasmid DNA containing the complete coding sequence of the CDCL1 gene as a probe for fluorescence in situ hybridization, Mincheva et al. (1994) mapped the gene to 3q21.

From its localization, CDCL1 became a candidate for an oncogene affected by chromosomal breaks in acute myeloid leukemia (AML). Tsuruga et al. (1997) reported the comparative analysis of the human MCM proteins MCM2, MCM3 (OMIM Ref. No. 602693), MCM5, and MCM7 (OMIM Ref. No. 600592). The 4 MCM proteins underwent unequal regulation, suggesting that they play somewhat distinct roles in the regulation of the mammalian cell cycle. The mRNA levels of these genes underwent cell cycle-dependent oscillations with a peak at G1/S phase; they may be regulated by E2F motifs (see OMIM Ref. No. E2F1; 189971), 2 of which were detected in the 5-prime regulatory region of the MCM5 gene. In contrast, the levels of these MCM proteins remained rather constant during the HeLa cell cycle. However, their levels gradually increased in a variable manner as normal cells progressed from G0 into the G1/S phase. In the G0 stage, the MCM2 and MCM5 proteins were much less abundant than the MCM7 and MCM3 proteins. This suggests that the MCM proteins are not present in stoichiometric amounts and that only a proportion of these molecules actively participate in cell cycle regulation as part of MCM complexes. Using an improved method for constructing conditional degron mu-



tants, Labib et al. (2000) demonstrated that depletion of minichromosome maintenance protein complexes after initiation irreversibly blocks the progression of replication forks in *S. cerevisiae*. Their experiments demonstrated that MCM complex is loaded at origins before initiation and is essential for elongation. Disruption of any one of the MCMs resulted in cells that were unable to complete the S phase, indicating that all MCM proteins are equally important for chromosome replication to continue after the activation of early origins of DNA replication. Labib et al. (2000) concluded that restricting MCM loading to the G1 phase ensures that initiation and elongation occur just once per cell cycle. Nomenclature: This gene has also been referred to as *cdc19* and D3S3194. See MCM7 (OMIM Ref. No. 600592), which also has been referred to as MCM2.

[66571] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66572] Blow, J. J.; Laskey, R. A. : A role for the nuclear envelope in controlling DNA replication within the cell cycle. *Nature* 332: 546–548, 1988. ; and

[66573] Burkhardt, R.; Schulte, D.; Hu, D.; Musahl, C.; Gohring, F.;

Knippers, R. : Interactions of human nuclear proteins P1Mcm3 and P1Cdc46. *Europ. J. Biochem.* 228: 431–438, 1995.

[66574] Further studies establishing the function and utilities of MCM2 are found in John Hopkins OMIM database record ID 116945, and in cited publications numbered 1923–1931 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Multiple Endocrine Neoplasia I (MEN1, Accession XM\_167804) is another VGAM1958 host target gene. MEN1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MEN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEN1 BINDING SITE, designated SEQ ID:44840, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66575] Another function of VGAM1958 is therefore inhibition of Multiple Endocrine Neoplasia I (MEN1, Accession XM\_167804). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEN1. Mesenchyme Homeo

Box 1 (MEOX1, Accession NM\_004527) is another VGAM1958 host target gene. MEOX1 BINDING SITE1 and MEOX1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MEOX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEOX1 BINDING SITE1 and MEOX1 BINDING SITE2, designated SEQ ID:10864 and SEQ ID:15188 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66576] Another function of VGAM1958 is therefore inhibition of Mesenchyme Homeo Box 1 (MEOX1, Accession NM\_004527), a gene which plays a role in mesoderm induction and isomitogenesis, and sclerotomal differentiation . Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEOX1. The function of MEOX1 has been established by previous studies. Using the technique of solution hybridization coupled with magnetic bead capture for the generation of a transcript map for the BRCA1 (OMIM Ref. No. 113705) region of 17q21,

Futreal et al. (1994) isolated the human homolog of the mouse Mox1 gene (termed MOX1 by them) which had previously been localized to a region of syntenic homology on mouse chromosome 11. MOX1 expression was observed in a variety of normal tissues examined, including breast and ovary. Because of this and because the gene contains a homeo box domain and has the potential to regulate growth and differentiation, MOX1 represented an attractive candidate for the BRCA1 gene. However, no evidence for mutation in the coding sequence was found in investigations of a series of BRCA1 kindreds and primary sporadic breast tumors. Nonetheless, the widespread expression of MOX1 in nonembryonic tissues suggests a role in normal cell biology. In the course of preparing a detailed physical and transcriptional map of the BRCA1 region, Jones et al. (1994) likewise located the MEOX1 gene, termed MOX1 by the authors. Another member of this gene family, MEOX2 (OMIM Ref. No. 600535), is located on chromosome 7p.

[66577] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66578] Futreal, P. A.; Cochran, C.; Rosenthal, J.; Miki, Y.; Swenson,

J.; Hobbs, M.; Bennett, L. M.; Haugen–Strano, A.; Marks, J.; Barrett, J. C.; Tavtigian, S. V.; Shattuck–Eidens, D.; Kamb, A.; Skolnick, M.; Wiseman, R. W. : Isolation of a diverged homeobox gene, MOX1, from the BRCA1 region on 17q21 by solution hybrid capture. Hum. Molec. Genet. 3: 1359–1364, 1994. ; and

[66579] Jones, K. A.; Black, D. M.; Brown, M. A.; Griffiths, B. L.; Nicolai, H. M.; Chambers, J. A.; Bonjardim, M.; Xu, C.–F.; Boyd, M.; McFarlane, R.; Korn, B.; Poustka, A.; North, M. A.; Scha.

[66580] Further studies establishing the function and utilities of MEOX1 are found in John Hopkins OMIM database record ID 600147, and in cited publications numbered 1335–1336 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mannosyl (alpha–1,6–)–glycoprotein Beta–1,6–N–acetyl–glucosaminyltransferase (MGAT5, Accession NM\_002410) is another VGAM1958 host target gene. MGAT5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGAT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of MGAT5 BINDING SITE, designated SEQ ID:8238, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66581] Another function of VGAM1958 is therefore inhibition of Mannosyl (alpha-1,6-)-glycoprotein Beta-1,6-N-acetyl-glucosaminyltransferase (MGAT5, Accession NM\_002410). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT5. Antigen Identified By Monoclonal Antibody Ki-67 (MKI67, Accession NM\_002417) is another VGAM1958 host target gene. MKI67 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MKI67, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKI67 BINDING SITE, designated SEQ ID:8255, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66582] Another function of VGAM1958 is therefore inhibition of Antigen Identified By Monoclonal Antibody Ki-67 (MKI67, Accession NM\_002417), a gene which thought to be re-

quired for maintaining cell proliferation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKI67. The function of MKI67 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM786. Matrix Metalloproteinase 15 (membrane-inserted) (MMP15, Accession NM\_002428) is another VGAM1958 host target gene. MMP15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MMP15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP15 BINDING SITE, designated SEQ ID:8265, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66583] Another function of VGAM1958 is therefore inhibition of Matrix Metalloproteinase 15 (membrane-inserted) (MMP15, Accession NM\_002428). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP15. MAX Binding Protein (MNT, Accession

NM\_020310) is another VGAM1958 host target gene. MNT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MNT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MNT BINDING SITE, designated SEQ ID:21558, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66584] Another function of VGAM1958 is therefore inhibition of MAX Binding Protein (MNT, Accession NM\_020310). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MNT. Myeloperoxidase (MPO, Accession NM\_000250) is another VGAM1958 host target gene. MPO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPO BINDING SITE, designated SEQ ID:5786, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.



[66585] Another function of VGAM1958 is therefore inhibition of Myeloperoxidase (MPO, Accession NM\_000250), a gene which is present in primary granules of neutrophilic granulocytes. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPO. The function of MPO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1915. Metallothionein-like 5, Testis-specific (tesmin) (MTL5, Accession NM\_004923) is another VGAM1958 host target gene. MTL5 BINDING SITE1 and MTL5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MTL5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTL5 BINDING SITE1 and MTL5 BINDING SITE2, designated SEQ ID:11359 and SEQ ID:11358 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66586] Another function of VGAM1958 is therefore inhibition of Metallothionein-like 5, Testis-specific (tesmin) (MTL5, Ac-

cession NM\_004923), a gene which functions in metal homeostasis and protects against heavy-metal toxicity. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTL5. The function of MTL5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM958. Myotubularin Related Protein 8 (MTMR8, Accession NM\_015458) is another VGAM1958 host target gene. MTMR8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTMR8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR8 BINDING SITE, designated SEQ ID:17748, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66587] Another function of VGAM1958 is therefore inhibition of Myotubularin Related Protein 8 (MTMR8, Accession NM\_015458), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with MTMR8. The function of MTMR8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM379. Myosin X (MYO10, Accession NM\_012334) is another VGAM1958 host target gene. MYO10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYO10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO10 BINDING SITE, designated SEQ ID:14729, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66588] Another function of VGAM1958 is therefore inhibition of Myosin X (MYO10, Accession NM\_012334), a gene which is an unconventional myosin. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO10. The function of MYO10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. N-acetylglucosaminidase, Alpha- (Sanfilippo

disease IIIB) (NAGLU, Accession NM\_000263) is another VGAM1958 host target gene. NAGLU BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NAGLU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAGLU BINDING SITE, designated SEQ ID:5804, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66589] Another function of VGAM1958 is therefore inhibition of N-acetylglucosaminidase, Alpha- (Sanfilippo disease IIIB) (NAGLU, Accession NM\_000263). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAGLU. N-ethylmaleimide-sensitive Factor Attachment Protein, Beta (NAPB, Accession XM\_046652) is another VGAM1958 host target gene. NAPB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NAPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAPB BINDING SITE, designated

SEQ ID:34769, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66590] Another function of VGAM1958 is therefore inhibition of N-ethylmaleimide-sensitive Factor Attachment Protein, Beta (NAPB, Accession XM\_046652). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAPB. Neuron Navigator 2 (NAV2, Accession XM\_012028) is another VGAM1958 host target gene. NAV2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAV2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAV2 BINDING SITE, designated SEQ ID:30206, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66591] Another function of VGAM1958 is therefore inhibition of Neuron Navigator 2 (NAV2, Accession XM\_012028), a gene which plays an important role in neuronal development, including neurite outgrowth. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with NAV2. The function of NAV2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM481. Neurocalcin Delta (NCALD, Accession NM\_032041) is another VGAM1958 host target gene. NCALD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCALD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCALD BINDING SITE, designated SEQ ID:25744, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66592] Another function of VGAM1958 is therefore inhibition of Neurocalcin Delta (NCALD, Accession NM\_032041). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCALD. Neural Cell Adhesion Molecule 1 (NCAM1, Accession NM\_000615) is another VGAM1958 host target gene. NCAM1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by NCAM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCAM1 BINDING SITE, designated SEQ ID:6216, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66593] Another function of VGAM1958 is therefore inhibition of Neural Cell Adhesion Molecule 1 (NCAM1, Accession NM\_000615), a gene which is involved in neuron–neuron adhesion, neurite fasciculation, outgrowth of neurites, etc. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCAM1. The function of NCAM1 has been established by previous studies. Because of evidence indicating close homology of neural cell adhesion molecule (NCAM) in man and mouse, a murine cDNA probe for NCAM could be used directly for in situ hybridization to human metaphase chromosomes (Nguyen et al., 1985). This procedure indicated that the NCAM gene is located at 11q22–q23. Mietus–Snyder et al. (1989) corroborated the location of the NCAM gene to the 11q23 region by finding linkage to the apolipoprotein gene clus–

ter, APOA1--APOC3--APOA4 (107680, 107720, 107690); a maximum lod score of 3.65 at  $\theta = 0.10$  was observed. Further studies by Mietus-Snyder et al. (1990) showed a maximum lod score of 15.9 at a recombination fraction of 0.028. D'Eustachio et al. (1985) mapped the NCAM gene to mouse chromosome 9 by means of a genomic probe in somatic cell hybrids. The gene is close to two others on mouse 9 whose expression is related to the nervous system, namely Thy-1 (see OMIM Ref. No. 188230 for the human counterpart) and the cerebellar connectional mutant staggerer (sg); NCAM-associated DNA polymorphisms were used in recombinant inbred strains of mice to show these linkages as well as close linkage to Sep-1 (apolipoprotein 1) and Lap-1 (leucine aminopeptidase 1). Great structural diversity in NCAM is due to transcriptional variations of a single gene and posttranslational mechanisms which are under exquisite developmental control (Rutishauser and Goridis, 1986). The neural cell adhesion molecule appears on early embryonic cells and is important in the formation of cell collectives and their boundaries at sites of morphogenesis. Later in development it is found on various differentiated tissues and is a major CAM mediating adhesion among



neurons and between neurons and muscle. NCAM is a membrane-bound glycoprotein that plays a role in cell-cell and cell-matrix adhesion through both its homophilic and heterophilic binding activity. To investigate the significance of this binding, Rabinowitz et al. (1996) used a gene targeting strategy in embryonic stem (ES) cells to replace the membrane-associated form of NCAM with a soluble, secreted form of its extracellular domain. Although the heterozygous mutant ES cells were able to generate low coat color chimeric mice, only the wildtype allele was transmitted, suggesting the possibility of dominant lethality. Analysis of chimeric embryos with a high level of ES cell contribution revealed severe growth retardation and morphologic defects by embryonic days 8.5–9.5. The second allele was also targeted and embryos derived almost entirely from the homozygous mutant ES cells exhibited the same lethal phenotype as observed with heterozygous chimeras

[66594] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66595] D'Eustachio, P.; Owens, G. C.; Edelman, G. M.; Cunningham, B. A. : Chromosomal location of the gene encoding

the neural cell adhesion molecule (N-CAM) in the mouse.

Proc. Nat. Acad. Sci. 82: 7631–7635, 1985. ; and

[66596] Rabinowitz, J. E.; Rutishauser, U.; Magnuson, T. : Targeted mutation of Ncam to produce a secreted molecule results in a dominant embryonic lethality. Proc. Nat. Acad. Sci. 93: 6421–64.

[66597] Further studies establishing the function and utilities of NCAM1 are found in John Hopkins OMIM database record ID 116930, and in cited publications numbered 11041, 12049–1205 and 12123–12130 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nuclear Receptor Coactivator 3 (NCOA3, Accession NM\_006534) is another VGAM1958 host target gene. NCOA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCOA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCOA3 BINDING SITE, designated SEQ ID:13282, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66598] Another function of VGAM1958 is therefore inhibition of

Nuclear Receptor Coactivator 3 (NCOA3, Accession NM\_006534), a gene which directly binds nuclear receptors and stimulates the transcriptional activities in hormone-dependent fashion. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCOA3. The function of NCOA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM215.N-myc Downstream Regulated Gene 1 (NDRG1, Accession XM\_005243) is another VGAM1958 host target gene. NDRG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDRG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG1 BINDING SITE, designated SEQ ID:29968, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66599] Another function of VGAM1958 is therefore inhibition of N-myc Downstream Regulated Gene 1 (NDRG1, Accession XM\_005243), a gene which may have a growth inhibitory

role. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG1. The function of NDRG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. Nuclear Factor of Activated T-cells, Cytoplasmic, Calcineurin-dependent 3 (NFATC3, Accession NM\_004555) is another VGAM1958 host target gene. NFATC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NFATC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFATC3 BINDING SITE, designated SEQ ID:10897, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66600] Another function of VGAM1958 is therefore inhibition of Nuclear Factor of Activated T-cells, Cytoplasmic, Calcineurin-dependent 3 (NFATC3, Accession NM\_004555), a gene which plays a role in the inducible expression of cytokine genes in t cells. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with NFATC3. The function of NFATC3 has been established by previous studies. The activation of NFAT proteins is controlled by calcineurin, the calmodulin-dependent phosphatase. Aramburu et al. (1998) identified a short conserved sequence in the NFATC3 protein (residues 110–122) that targets calcineurin to NFAT. Mutation of a single residue in this sequence impairs the calcineurin-mediated dephosphorylation and nuclear translocation of NFAT1. Peptides spanning the region inhibit the ability of calcineurin to bind to and dephosphorylate NFAT proteins, without affecting the phosphatase activity of calcineurin against other substrates. When expressed intracellularly, a corresponding peptide inhibits NFAT dephosphorylation, nuclear translocation, and NFAT-mediated expression in response to stimulation. Thus, disruption of the enzyme-substrate docking interaction that directs calcineurin to NFAT can effectively block NFAT-dependent functions. Animal model experiments lend further support to the function of NFATC3. Rengarajan et al. (2002) generated *Nfatc2* and *Nfatc3* double-knockout (DKO) mice. They found that *Nfatc2* and *Nfatc3* are critical in the determination of the fate of precursor T helper (Th) cells. DKO T cells intrinsi-

cally differentiated into Th2 cytokine-secreting cells, even in the absence of IL4 (OMIM Ref. No. 147780). Treatment of DKO mice with IL12 (OMIM Ref. No. 161561) and anti-IL4, however, enabled the cells to become gamma-interferon (IFNG; 147570)-secreting Th1 lymphocytes. In addition, the cells from the DKO mice were hyperresponsive to T-cell receptor (TCR; OMIM Ref. No. 186880)-mediated activation and did not require the engagement of the accessory receptor, CD28 (OMIM Ref. No. 186760), for proliferation.

[66601] It is appreciated that the abovementioned animal model for NFATC3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[66602] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66603] Rengarajan, J.; Tang, B.; Glimcher, L. H. : NFATc2 and NFATc3 regulate TH2 differentiation and modulate TCR-responsiveness of naive TH cells. *Nature Immun.* 3: 48-54, 2002. ; and

[66604] Aramburu, J.; Garcia-Cozar, F.; Raghavan, A.; Okamura, H.; Rao, A.; Hogan, P. G. : Selective inhibition of NFAT activation by a peptide spanning the calcineurin targeting

site of NFAT. Mol.

[66605] Further studies establishing the function and utilities of NFATC3 are found in John Hopkins OMIM database record ID 602698, and in cited publications numbered 9903, 7968, 990 and 10195 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nuclear Factor (erythroid-derived 2), 45kDa (NFE2, Accession NM\_006163) is another VGAM1958 host target gene. NFE2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NFE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFE2 BINDING SITE, designated SEQ ID:12818, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66606] Another function of VGAM1958 is therefore inhibition of Nuclear Factor (erythroid-derived 2), 45kDa (NFE2, Accession NM\_006163), a gene which regulates expression of the beta globin gene. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFE2. The function of NFE2 has been established by previous studies. Peters

et al. (1993) demonstrated that the Nfe2 gene in the mouse maps to chromosome 15 in a region containing the microcytic anemia (mk) gene. Homozygous mk mice were shown by Bannerman et al. (1972) to have defective intestinal iron transport and severe anemia. Peters et al. (1993) demonstrated Nfe2 expression in the mouse small intestine and NF-E2 binding activity in nuclear extracts of a human colon carcinoma cell line (OMIM Ref. No. Caco-2). Caco-2 cells possess properties of the small intestine, including the ability to transport iron. These data together indicated that NF-E2 plays a role in all aspects of hemoglobin production: globin synthesis, heme synthesis, and the procurement of iron. (NF-E2 recognition sites are present not only in the locus control regions of the globin genes but also in the gene promoters of 2 heme biosynthetic enzymes, uroporphobilinogen deaminase (OMIM Ref. No. 176000) and ferrochelatase (OMIM Ref. No. 177000).) The 45-kD subunit of the human globin locus control region binding protein, NFE2, was cloned by homology to the murine gene. Immunoprecipitation experiments demonstrated in vivo association of the p45 subunit with an 18-kD protein (see OMIM Ref. No. MAFG, 602020, and MAFK, 600197). Because bZIP proteins bind DNA as



dimers, it is likely that native NFE2 is a heterodimer of 45- and 18-kD subunits. By fluorescence in situ hybridization, Weremowicz et al. (1993) assigned the p45 subunit of NFE2 to 12q13. Chan et al. (1993) likewise cloned the human homolog of mouse NF-E2. Extensive survey of human tissue samples found that NFE2 expression is not limited to erythropoietic organs. Expression in the colon and testis suggested that NFE2 may participate in the regulation of genes other than globin

[66607] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66608] Shivdasani, R. A.; Rosenblatt, M. F.; Zucker-Franklin, D.; Jackson, C. W.; Hunt, P.; Saris, C. J. M.; Orkin, S. H. : Transcription factor NF-E2 is required for platelet formation independent of the actions of thrombopoietin/MGDF in megakaryocyte development. Cell 81: 695-704, 1995. ; and

[66609] Weremowicz, S.; Andrews, N. C.; Orkin, S. H.; Morton, C. C. : Mapping the p45 subunit of human NFE2 to 12q13. (Abstract) Human Genome Mapping Workshop 93 25, 1993.

[66610] Further studies establishing the function and utilities of

NFE2 are found in John Hopkins OMIM database record ID 601490, and in cited publications numbered 998 and 10585–1274 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nuclear Factor (erythroid–derived 2)–like 1 (NFE2L1, Accession NM\_003204) is another VGAM1958 host target gene. NFE2L1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NFE2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFE2L1 BINDING SITE, designated SEQ ID:9197, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66611] Another function of VGAM1958 is therefore inhibition of Nuclear Factor (erythroid–derived 2)–like 1 (NFE2L1, Accession NM\_003204), a gene which may regulate expression of ferritin genes. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFE2L1. The function of NFE2L1 and its association with various diseases and clinical conditions, has been established by previous

studies, as described hereinabove with reference to VGAM369.NKX3A (Accession NM\_006167) is another VGAM1958 host target gene. NKX3A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NKX3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NKX3A BINDING SITE, designated SEQ ID:12828, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66612] Another function of VGAM1958 is therefore inhibition of NKX3A (Accession NM\_006167), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NKX3A. The function of NKX3A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM481.Neuronal Pentraxin I (NPTX1, Accession NM\_002522) is another VGAM1958 host target gene. NPTX1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by NPTX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPTX1 BINDING SITE, designated SEQ ID:8357, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66613] Another function of VGAM1958 is therefore inhibition of Neuronal Pentraxin I (NPTX1, Accession NM\_002522), a gene which may be involved in synaptic uptake of extracellular material and is very strongly similar to rat NP1. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPTX1. The function of NPTX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM111. Nuclear Receptor Subfamily 4, Group A, Member 2 (NR4A2, Accession NM\_006186) is another VGAM1958 host target gene. NR4A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NR4A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of NR4A2 BINDING SITE, designated SEQ ID:12857, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66614] Another function of VGAM1958 is therefore inhibition of Nuclear Receptor Subfamily 4, Group A, Member 2 (NR4A2, Accession NM\_006186), a gene which may be a general coactivator of transcription. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR4A2. The function of NR4A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM127.Nebulin-related Anchoring Protein (Nrap, Accession NM\_139235) is another VGAM1958 host target gene. Nrap BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Nrap, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Nrap BINDING SITE, designated SEQ ID:29236, to the nucleotide sequence of VGAM1958 RNA,

herein designated VGAM RNA, also designated SEQ ID:4669.

[66615] Another function of VGAM1958 is therefore inhibition of Nebulin-related Anchoring Protein (Nrap, Accession NM\_139235), a gene which performs an anchoring function to link the terminal actin filaments of myofibrils to protein complexes located beneath the sarcolemma. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Nrap. The function of Nrap and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM649. Neurotrophic Tyrosine Kinase, Receptor, Type 2 (NTRK2, Accession NM\_006180) is another VGAM1958 host target gene. NTRK2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NTRK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTRK2 BINDING SITE, designated SEQ ID:12846, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ

ID:4669.

[66616] Another function of VGAM1958 is therefore inhibition of Neurotrophic Tyrosine Kinase, Receptor, Type 2 (NTRK2, Accession NM\_006180), a gene which is involved in the development and/or maintenance of the nervous system. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTRK2. The function of NTRK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM341. Nucleobindin 1 (NUCB1, Accession NM\_006184) is another VGAM1958 host target gene. NUCB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUCB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUCB1 BINDING SITE, designated SEQ ID:12852, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66617] Another function of VGAM1958 is therefore inhibition of Nucleobindin 1 (NUCB1, Accession NM\_006184), a gene

which may have a role in calcium homeostasis. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUCB1. The function of NUCB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1523. Nuclear Mitotic Apparatus Protein 1 (NUMA1, Accession XM\_167853) is another VGAM1958 host target gene. NUMA1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NUMA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUMA1 BINDING SITE, designated SEQ ID:44883, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66618] Another function of VGAM1958 is therefore inhibition of Nuclear Mitotic Apparatus Protein 1 (NUMA1, Accession XM\_167853), a gene which is nuclear mitotic apparatus protein. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUMA1. The function of



NUMA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM192. Nucleoporin 98kDa (NUP98, Accession NM\_016320) is another VGAM1958 host target gene. NUP98 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUP98, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUP98 BINDING SITE, designated SEQ ID:18444, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66619] Another function of VGAM1958 is therefore inhibition of Nucleoporin 98kDa (NUP98, Accession NM\_016320), a gene which functions in the nuclear transport of protein and RNA. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUP98. The function of NUP98 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM55.2'-5'-oligoadenylate Synthetase 2, 69/71kDa (OAS2, Accession NM\_002535) is another VGAM1958 host target gene. OAS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAS2 BINDING SITE, designated SEQ ID:8374, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66620] Another function of VGAM1958 is therefore inhibition of 2'-5'-oligoadenylate Synthetase 2, 69/71kDa (OAS2, Accession NM\_002535), a gene which may play a role in mediating resistance to virus infection, control of cell growth, differentiation, and apoptosis. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAS2. The function of OAS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1498.O-linked N-acetylglucosamine (GlcNAc) Transferase

(UDP-N-acetylglucosamine:polypeptide-N-acetylglucosaminyl transferase) (OGT, Accession NM\_003605) is another VGAM1958 host target gene. OGT BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OGT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OGT BINDING SITE, designated SEQ ID:9662, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66621] Another function of VGAM1958 is therefore inhibition of O-linked N-acetylglucosamine (GlcNAc) Transferase (UDP-N-acetylglucosamine:polypeptide-N-acetylglucosaminyl transferase) (OGT, Accession NM\_003605), a gene which has a role in the glycosylation of nuclear and cytoplasmic proteins. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OGT. The function of OGT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM464.Oligodendrocyte Lineage Transcription Factor 2

(OLIG2, Accession NM\_005806) is another VGAM1958 host target gene. OLIG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OLIG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OLIG2 BINDING SITE, designated SEQ ID:12381, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66622] Another function of VGAM1958 is therefore inhibition of Oligodendrocyte Lineage Transcription Factor 2 (OLIG2, Accession NM\_005806), a gene which may bind DNA and contains a helix-loop-helix DNA-binding domain. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OLIG2. The function of OLIG2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1514. Oligophrenin 1 (OPHN1, Accession NM\_002547) is another VGAM1958 host target gene. OPHN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by OPHN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPHN1 BINDING SITE, designated SEQ ID:8401, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66623] Another function of VGAM1958 is therefore inhibition of Oligophrenin 1 (OPHN1, Accession NM\_002547). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPHN1. Otoferlin (OTOF, Accession NM\_004802) is another VGAM1958 host target gene. OTOF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OTOF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OTOF BINDING SITE, designated SEQ ID:11225, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66624] Another function of VGAM1958 is therefore inhibition of Otoferlin (OTOF, Accession NM\_004802), a gene which is

involved in vesicle membrane fusion and required for inner ear function. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OTOF. The function of OTOF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM625. Protein Kinase C and Casein Kinase Substrate In Neurons 1 (PACSIN1, Accession XM\_166424) is another VGAM1958 host target gene. PACSIN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACSIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACSIN1 BINDING SITE, designated SEQ ID:44315, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66625] Another function of VGAM1958 is therefore inhibition of Protein Kinase C and Casein Kinase Substrate In Neurons 1 (PACSIN1, Accession XM\_166424). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAC-

SIN1. Phosphoribosylaminoimidazole Carboxylase, Phosphoribosylaminoimidazole Succinocarboxamide Synthetase (PAICS, Accession NM\_006452) is another VGAM1958 host target gene. PAICS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PAICS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAICS BINDING SITE, designated SEQ ID:13163, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66626] Another function of VGAM1958 is therefore inhibition of Phosphoribosylaminoimidazole Carboxylase, Phosphoribosylaminoimidazole Succinocarboxamide Synthetase (PAICS, Accession NM\_006452), a gene which is required for purine biosynthesis. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAICS. The function of PAICS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM894.PART1 (Accession NM\_016590) is another

VGAM1958 host target gene. PART1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PART1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PART1 BINDING SITE, designated SEQ ID:18666, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66627] Another function of VGAM1958 is therefore inhibition of PART1 (Accession NM\_016590). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PART1. Prostatic Binding Protein (PBP, Accession NM\_002567) is another VGAM1958 host target gene. PBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PBP BINDING SITE, designated SEQ ID:8415, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.



[66628] Another function of VGAM1958 is therefore inhibition of Prostatic Binding Protein (PBP, Accession NM\_002567), a gene which regulates the activity of the Raf/MEK/ERK module. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PBP. The function of PBP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1332. Protocadherin Beta 16 (PCDHB16, Accession NM\_020957) is another VGAM1958 host target gene. PCDHB16 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PCDHB16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB16 BINDING SITE, designated SEQ ID:21943, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66629] Another function of VGAM1958 is therefore inhibition of Protocadherin Beta 16 (PCDHB16, Accession NM\_020957), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1958 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHB16. The function of PCDHB16 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM931.6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (PFKFB3, Accession XM\_096349) is another VGAM1958 host target gene. PFKFB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PFKFB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PFKFB3 BINDING SITE, designated SEQ ID:40318, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66630] Another function of VGAM1958 is therefore inhibition of 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (PFKFB3, Accession XM\_096349), a gene which catalyzes synthesis and degradation of fructose 2,6-bisphosphate. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PFKFB3. The function of PFKFB3 has

been established by previous studies. The bifunctional 6-phosphofructo-2-kinase (EC 2.7.1.105)/fructose-2,6-bisphosphatase (EC 3.1.3.46) (PFKFB) regulates the steady-state concentration of fructose-2,6-bisphosphate, a potent activator of a key regulatory enzyme of glycolysis, phosphofructokinase. Cancer cells maintain a high glycolytic rate even in the presence of oxygen, a phenomenon known as the Warburg effect (Warburg, 1956). The glycolytic rate in the placenta, another fast-growing tissue, is accelerated by anoxia and by maternal diabetes. By screening a placental cDNA library with human and frog liver PFKFB (PFKFB1; 311790) as probes, Sakai et al. (1996) obtained a cDNA encoding PFKFB3, which they termed HP (human placental PFKFB). The predicted PFKFB3 protein, which is 61% similar to human liver PFKFB, contains 529 amino acids and 7 potential phosphorylation sites. Northern blot analysis of first-trimester and term placentas detected a 4.5-kb PFKFB3 transcript

[66631] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66632] Sakai, A.; Kato, M.; Fukasawa, M.; Ishiguro, M.; Furuya, E.;

Sakakibara, R. : Cloning of cDNA encoding for a novel isozyme of fructose 6-phosphate,2-kinase/fructose 2,6-bisphosphatase from human placenta. J. Biochem. 119: 506-511, 1996. ; and

[66633] Warburg, O. : On the origin of cancer cells. Science 123: 309-314, 1956.

[66634] Further studies establishing the function and utilities of PFKFB3 are found in John Hopkins OMIM database record ID 605319, and in cited publications numbered 4485-4488, 449 and 7350 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM\_027982) is another VGAM1958 host target gene. PIK3R3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3R3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3R3 BINDING SITE, designated SEQ ID:30605, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66635] Another function of VGAM1958 is therefore inhibition of Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM\_027982). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3R3. Polycystic Kidney Disease 1 (autosomal dominant) (PKD1, Accession NM\_000296) is another VGAM1958 host target gene. PKD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PKD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKD1 BINDING SITE, designated SEQ ID:5841, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66636] Another function of VGAM1958 is therefore inhibition of Polycystic Kidney Disease 1 (autosomal dominant) (PKD1, Accession NM\_000296). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKD1. Phospholipase A2, Group IID (PLA2G2D, Accession NM\_012400) is another VGAM1958 host target gene.

PLA2G2D BINDING SITE1 and PLA2G2D BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PLA2G2D, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2G2D BINDING SITE1 and PLA2G2D BINDING SITE2, designated SEQ ID:14772 and SEQ ID:14769 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66637] Another function of VGAM1958 is therefore inhibition of Phospholipase A2, Group IID (PLA2G2D, Accession NM\_012400), a gene which is involved in phospholipid digestion, remodeling of cell membranes, and host defense, as well as pathophysiologic processes. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLA2G2D. The function of PLA2G2D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Phospholipase C, Beta 2 (PLCB2, Accession NM\_004573) is another VGAM1958 host target gene. PLCB2 BINDING SITE is HOST TARGET

binding site found in the 5` untranslated region of mRNA encoded by PLCB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLCB2 BINDING SITE, designated SEQ ID:10916, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66638] Another function of VGAM1958 is therefore inhibition of Phospholipase C, Beta 2 (PLCB2, Accession NM\_004573), a gene which is the beta 2 subunit of phospholipase C. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLCB2. The function of PLCB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1188. Protein Phosphatase 1, Catalytic Subunit, Beta Isoform (PPP1CB, Accession NM\_002709) is another VGAM1958 host target gene. PPP1CB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPP1CB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of PPP1CB BINDING SITE, designated SEQ ID:8556, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66639] Another function of VGAM1958 is therefore inhibition of Protein Phosphatase 1, Catalytic Subunit, Beta Isoform (PPP1CB, Accession NM\_002709), a gene which is the catalytic subunit of protein phosphatase 1. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1CB. The function of PPP1CB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM46. Protein Phosphatase 2, Regulatory Subunit B (B56), Alpha Isoform (PPP2R5A, Accession NM\_006243) is another VGAM1958 host target gene. PPP2R5A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP2R5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R5A BINDING SITE, designated SEQ



ID:12909, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66640] Another function of VGAM1958 is therefore inhibition of Protein Phosphatase 2, Regulatory Subunit B (B56), Alpha Isoform (PPP2R5A, Accession NM\_006243), a gene which is a regulatory subunit of protein phosphatase 2A. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R5A. The function of PPP2R5A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675. Palmitoyl-protein Thioesterase 1 (ceroid-lipofuscinosis, neuronal 1, infantile) (PPT1, Accession XM\_029842) is another VGAM1958 host target gene. PPT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPT1 BINDING SITE, designated SEQ ID:30956, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ

ID:4669.

[66641] Another function of VGAM1958 is therefore inhibition of Palmitoyl-protein Thioesterase 1 (ceroid-lipofuscinosis, neuronal 1, infantile) (PPT1, Accession XM\_029842). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPT1. Protein Kinase C, Alpha Binding Protein (PRKCABP, Accession NM\_012407) is another VGAM1958 host target gene. PRKCABP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRKCABP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKCABP BINDING SITE, designated SEQ ID:14787, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66642] Another function of VGAM1958 is therefore inhibition of Protein Kinase C, Alpha Binding Protein (PRKCABP, Accession NM\_012407), a gene which may interact with the catalytic domain of protein C kinase. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRK-

CABP. The function of PRKCABP has been established by previous studies. Staudinger et al. (1995) obtained a mouse cDNA encoding Prkcabp, which they called Pick1 (protein interacting with C kinase-1), using a yeast 2-hybrid screen with the catalytic domain of the alpha isoform of activated protein kinase C (PRKCA; 176960) as bait. Immunofluorescence microscopy demonstrated intense perinuclear and diffuse cytoplasmic staining. Using a yeast 2-hybrid screen of a B-cell cDNA library with p67-phox (NCF2; 233710) as bait, Takeya et al. (2000) obtained a cDNA encoding human PRKCABP, which they called PICK1. Sequence analysis predicted that the 415-amino acid protein, which is 92% identical to the mouse protein, contains an N-terminal PDZ domain and a conserved arfaptin homology (AH) domain (see OMIM Ref. No. 601638). Northern blot analysis revealed ubiquitous expression of a 2.0-kb PICK1 transcript. Genomic sequence analysis determined that the PICK1 gene contains 13 exons and spans at least 18 kb. Yeast 2-hybrid analysis indicated that the PDZ domain, but not the AH domain, of PICK1 interacts with the C termini of the GTP-bound forms of ADP-ribosylation factor-1 (ARF1; 103180) and ARF3 (OMIM Ref. No. 103190). The interaction with ARF5

(OMIM Ref. No. 103188) and ARF6 (OMIM Ref. No. 600464) was weak, suggesting that the PICK1 interaction is specific for class I ARFs and that it may regulate Golgi-to-endoplasmic reticulum vesicle transport. Dev et al. (1999) showed that the PDZ domain of rat Pick1 interacts with the last 10 amino acids of the short C-terminal alternative splice variants of AMPA receptor subunits (e.g., GLUR2; 138248). They proposed that E-S-V/I-K-I, a sequence found in these 10 amino acids, is a novel PDZ-binding motif. Dev et al. (1999) noted that PRKCA phosphorylates Pick1 efficiently but binds Pick1 in both the phosphorylated and unphosphorylated states. Xia et al. (1999) reported that Pick1 interacts with mouse AMPA glutamate receptors and noted their colocalization at excitatory synapses in the brain. Using a yeast 2-hybrid system, Cowan et al. (2000) demonstrated that mouse Pick1 binds the C-terminal tail of Ephb2 (OMIM Ref. No. 600997). Metabotropic glutamate receptor-7 (mGluR7; 604101) localizes specifically to presynaptic active zones. Boudin et al. (2000) showed that the extreme C-terminal 3 amino acids of mGluR7 interact with the PDZ domain of Pick1. Immunofluorescence microscopy demonstrated that both proteins are localized at excitatory synapses in hip-

pocampal neurons. The authors showed that the clustering of mGluR7 at synapses requires its C-terminal PDZ-binding residues. Mutant mGluR7 lacking the PDZ-binding residues localized diffusely along axons rather than at the synapse, suggesting a role for Pick1 as a scaffolding molecule at presynaptic sites. By its inclusion within a mapped clone, Takeya et al. (2000) mapped the PRKCABP gene to 22q12.3–q13.2.

[66643] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66644] Boudin, H.; Doan, A.; Xia, J.; Shigemoto, R.; Huganir, R. L.; Worley, P.; Craig, A. M. : Presynaptic clustering of mGluR7a requires the PICK1 PDZ domain binding site. Neuron 28: 485–497, 2000. ; and

[66645] Cowan, C. A.; Yokoyama, N.; Bianchi, L. M.; Henkemeyer, M.; Fritzsche, B. : EphB2 guides axons at the midline and is necessary for normal vestibular function. Neuron 26: 417–430, 2000.

[66646] Further studies establishing the function and utilities of PRKCABP are found in John Hopkins OMIM database record ID 605926, and in cited publications numbered 644 and 12328–6444 listed in the bibliography section

hereinbelow, which are also hereby incorporated by reference. Prostaglandin F Receptor (FP) (PTGFR, Accession NM\_000959) is another VGAM1958 host target gene. PTGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGFR BINDING SITE, designated SEQ ID:6664, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66647] Another function of VGAM1958 is therefore inhibition of Prostaglandin F Receptor (FP) (PTGFR, Accession NM\_000959), a gene which mediates intracellular calcium flux, strongly similar to murine *Ptgfr*. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGFR. The function of PTGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1781. Prostaglandin-endoperoxide Synthase 1 (prostaglandin G/H synthase and cyclooxygenase) (PTGS1, Accession NM\_000962) is another VGAM1958

host target gene. PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTGS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2, designated SEQ ID:6674 and SEQ ID:27895 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66648] Another function of VGAM1958 is therefore inhibition of Prostaglandin-endoperoxide Synthase 1 (prostaglandin G/H synthase and cyclooxygenase) (PTGS1, Accession NM\_000962), a gene which may play an important role in regulating or promoting cell proliferation in some normal and neoplastically transformed cells. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGS1. The function of PTGS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. Protein Tyrosine Phosphatase, Non-receptor Type 11 (Noonan syndrome 1) (PTPN11, Ac-

cession NM\_002834) is another VGAM1958 host target gene. PTPN11 BINDING SITE1 and PTPN11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPN11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPN11 BINDING SITE1 and PTPN11 BINDING SITE2, designated SEQ ID:8712 and SEQ ID:10539 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66649] Another function of VGAM1958 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type 11 (Noonan syndrome 1) (PTPN11, Accession NM\_002834). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPN11. Phosphorylase, Glycogen; Brain (PYGB, Accession NM\_002862) is another VGAM1958 host target gene. PYGB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PYGB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the



nucleotide sequences of PYGB BINDING SITE, designated SEQ ID:8764, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66650] Another function of VGAM1958 is therefore inhibition of Phosphorylase, Glycogen; Brain (PYGB, Accession NM\_002862). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYGB. PYGO2 (Accession XM\_034083) is another VGAM1958 host target gene. PYGO2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PYGO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYGO2 BINDING SITE, designated SEQ ID:32000, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66651] Another function of VGAM1958 is therefore inhibition of PYGO2 (Accession XM\_034083). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYGO2.

RAB, Member of RAS Oncogene Family-like 2A (RABL2A, Accession NM\_013412) is another VGAM1958 host target gene. RABL2A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RABL2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RABL2A BINDING SITE, designated SEQ ID:15077, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66652] Another function of VGAM1958 is therefore inhibition of RAB, Member of RAS Oncogene Family-like 2A (RABL2A, Accession NM\_013412). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RABL2A. RAB, Member of RAS Oncogene Family-like 2B (RABL2B, Accession NM\_007081) is another VGAM1958 host target gene. RABL2B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RABL2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of RABL2B BINDING SITE, designated SEQ ID:13944, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66653] Another function of VGAM1958 is therefore inhibition of RAB, Member of RAS Oncogene Family-like 2B (RABL2B, Accession NM\_007081). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RABL2B. RAD1 Homolog (*S. pombe*) (RAD1, Accession NM\_133377) is another VGAM1958 host target gene. RAD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD1 BINDING SITE, designated SEQ ID:28499, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66654] Another function of VGAM1958 is therefore inhibition of RAD1 Homolog (*S. pombe*) (RAD1, Accession NM\_133377), a gene which has important roles in DNA damage-activated mitotic and meiotic cell cycle check-

points. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD1. The function of RAD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM922.RAD54-like (*S. cerevisiae*) (RAD54L, Accession NM\_003579) is another VGAM1958 host target gene. RAD54L BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAD54L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD54L BINDING SITE, designated SEQ ID:9629, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66655] Another function of VGAM1958 is therefore inhibition of RAD54-like (*S. cerevisiae*) (RAD54L, Accession NM\_003579), a gene which is involved in dna repair and mitotic recombination. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD54L. The func-

tion of RAD54L has been established by previous studies. Repair of double-stranded DNA breaks is essential for homologous recombination in somatic cells to protect DNA from damage by ionizing radiation and other genotoxins. The rad52 pathway is required for homologous recombination in the yeast *S. cerevisiae*. Kanaar et al. (1996) searched for mammalian homologs of yeast rad54, an essential component of this pathway and a member of the rad52 group. Using RT-PCR with degenerate primers, Kanaar et al. (1996) identified the mouse and human homologs of *S. cerevisiae* rad54. The human homolog, HR54, is 48% identical to the yeast protein and belongs to the SNF2/SWI2 family, which is characterized by amino acid motifs found in DNA-dependent ATPases. Proteins in the SNF2/SWI2 family are involved in many aspects of DNA metabolism, including transcription, repair, and recombination. HR54 protein is located in the nucleus, consistent with its nuclear localization signal and a potential function in DNA metabolism. Expression of HR54 increased approximately 3-fold in late G1 phase; this pattern is similar to that in yeast. HR54 was able to partially complement the DNA repair defect of *S. cerevisiae* rad54-deleted cells. By Northern blot analysis, Kanaar et al. (1996) showed

that expression of the mouse homolog of HR54 is increased in organs of lymphoid and germ cell development. Mouse expression was 3-fold higher in spermatocytes than in spermatids, suggesting that HR54 plays a role in meiotic recombination. Kanaar et al. (1996) mapped the HR54 gene to chromosome 1p32 using fluorescence in situ hybridization. Association of the recombinational repair protein RAD51 (OMIM Ref. No. 179617) with tumor suppressors BRCA1 (OMIM Ref. No. 113705) and BRCA2 (OMIM Ref. No. 600185) suggested that defects in homologous recombination are responsible for tumor formation. This idea was supported by the fact that the protein associated with the MRE11/RAD50 repair complex (NBS1; 602667) is mutated in Nijmegen breakage syndrome (OMIM Ref. No. 251260), which is characterized by increased cancer incidence and sensitivity to ionizing radiation. Since RAD51 forms a complex with other members of the RAD52 (OMIM Ref. No. 600392) epistasis group and with BRCA proteins, it was reasonable to ask if alterations of members of the RAD52 epistasis group lead to tumor development. Matsuda et al. (1999) described missense mutations at functional regions of RAD54 and the absence of the wildtype RAD54 expression resulting

from aberrant splicing in primary cancers. Since RAD54 is a recombination protein associated with RAD51, this was the first genetic evidence that cancer can arise from a defect in repair processes involving homologous recombination. They observed a pro63-to-his mutation (603615.0001) of the RAD54 gene in an adenocarcinoma of the colon and a val444-to-glu mutation (603615.0002) in a non-Hodgkin lymphoma. Although pro at codon 63 and val at codon 444 are outside helicase motifs, Matsuda et al. (1999) considered it likely that these amino acid substitutions affect the function of RAD54. The mutations demonstrated by Matsuda et al. (1999) were rare among the tumors studied: 95 breast cancers, 13 colorectal cancers, and 24 lymphomas.

[66656] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66657] Kanaar, R.; Troelstra, C.; Swagemakers, S. M. A.; Essers, J.; Smit, B.; Franssen, J.-H.; Pastink, A.; Bezzubova, O. Y.; Buerstedde, J.-M.; Clever, B.; Heyer, W.-D.; Hoeijmakers, J. H. J. : Human and mouse homologs of the *Saccharomyces cerevisiae* RAD54 DNA repair gene: evidence for functional conservation. *Curr. Biol.* 6: 828–838, 1996. ; and

[66658] Matsuda, M.; Miyagawa, K.; Takahashi, M.; Fukuda, T.; Kataoka, T.; Asahara, T.; Inui, H.; Watatani, M.; Yasutomi, M.; Kamada, N.; Dohi, K.; Kamiya, K. : Mutations in the RAD54 recombina.

[66659] Further studies establishing the function and utilities of RAD54L are found in John Hopkins OMIM database record ID 603615, and in cited publications numbered 7589–7590 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Retinoic Acid Induced 3 (RAI3, Accession NM\_003979) is another VGAM1958 host target gene. RAI3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI3 BINDING SITE, designated SEQ ID:10115, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66660] Another function of VGAM1958 is therefore inhibition of Retinoic Acid Induced 3 (RAI3, Accession NM\_003979). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical condi-



tions associated with RAI3. RalA Binding Protein 1 (RALBP1, Accession NM\_006788) is another VGAM1958 host target gene. RALBP1 BINDING SITE1 and RALBP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RALBP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RALBP1 BINDING SITE1 and RALBP1 BINDING SITE2, designated SEQ ID:13660 and SEQ ID:13662 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66661] Another function of VGAM1958 is therefore inhibition of RalA Binding Protein 1 (RALBP1, Accession NM\_006788), a gene which plays a role in signal transduction and catalyzes the transport of glutathione conjugates and xenobiotics. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RALBP1. The function of RALBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM345.RecQ Protein-like 5 (RECQL5, Accession

NM\_004259) is another VGAM1958 host target gene. RECQL5 BINDING SITE1 and RECQL5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RECQL5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RECQL5 BINDING SITE1 and RECQL5 BINDING SITE2, designated SEQ ID:10449 and SEQ ID:10448 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66662] Another function of VGAM1958 is therefore inhibition of RecQ Protein-like 5 (RECQL5, Accession NM\_004259). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RECQL5. Arginine-glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM\_012102) is another VGAM1958 host target gene. RERE BINDING SITE1 and RERE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RERE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

RERE BINDING SITE1 and RERE BINDING SITE2, designated SEQ ID:14408 and SEQ ID:13261 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66663] Another function of VGAM1958 is therefore inhibition of Arginine–glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM\_012102), a gene which binds DRPLA and locates in the nucleus. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RERE. The function of RERE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51. Ribulose–5–phosphate–3–epimerase (RPE, Accession XM\_030834) is another VGAM1958 host target gene. RPE BINDING SITE1 and RPE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RPE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPE BINDING SITE1 and RPE BINDING SITE2, designated SEQ ID:31156 and SEQ ID:31154 respectively, to the nucleotide sequence of

VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66664] Another function of VGAM1958 is therefore inhibition of Ribulose-5-phosphate-3-epimerase (RPE, Accession XM\_030834). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPE. Sal-like 2 (Drosophila) (SALL2, Accession XM\_033473) is another VGAM1958 host target gene. SALL2 BINDING SITE1 and SALL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SALL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SALL2 BINDING SITE1 and SALL2 BINDING SITE2, designated SEQ ID:31935 and SEQ ID:31936 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66665] Another function of VGAM1958 is therefore inhibition of Sal-like 2 (Drosophila) (SALL2, Accession XM\_033473). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SALL2. Succinate Dehydrogenase

Complex, Subunit C, Integral Membrane Protein, 15kDa (SDHC, Accession XM\_045183) is another VGAM1958 host target gene. SDHC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SDHC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDHC BINDING SITE, designated SEQ ID:34381, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66666] Another function of VGAM1958 is therefore inhibition of Succinate Dehydrogenase Complex, Subunit C, Integral Membrane Protein, 15kDa (SDHC, Accession XM\_045183). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDHC. Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 13 (SERPINB13, Accession NM\_012397) is another VGAM1958 host target gene. SERPINB13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SERPINB13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERPINB13 BINDING SITE, designated SEQ ID:14761, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66667] Another function of VGAM1958 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 13 (SERPINB13, Accession NM\_012397), a gene which plays a role in the proliferation or differentiation of keratinocytes. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERPINB13. The function of SERPINB13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1924. Soc-2 Suppressor of Clear Homolog (C. elegans) (SHOC2, Accession NM\_007373) is another VGAM1958 host target gene. SHOC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SHOC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

SHOC2 BINDING SITE, designated SEQ ID:14303, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66668] Another function of VGAM1958 is therefore inhibition of Soc-2 Suppressor of Clear Homolog (*C. elegans*) (SHOC2, Accession NM\_007373), a gene which may be a regulator of the let-60 ras pathway. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHOC2. The function of SHOC2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM464. Short Stature Homeobox (SHOX, Accession NM\_000451) is another VGAM1958 host target gene. SHOX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SHOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHOX BINDING SITE, designated SEQ ID:6055, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66669] Another function of VGAM1958 is therefore inhibition of

Short Stature Homeobox (SHOX, Accession NM\_000451). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHOX. Single-minded Homolog 1 (Drosophila) (SIM1, Accession NM\_005068) is another VGAM1958 host target gene. SIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIM1 BINDING SITE, designated SEQ ID:11511, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66670] Another function of VGAM1958 is therefore inhibition of Single-minded Homolog 1 (Drosophila) (SIM1, Accession NM\_005068), a gene which may have pleiotropic effects during embryogenesis and in the adult. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIM1. The function of SIM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with



reference to VGAM665.Solute Carrier Family 16 (monocarboxylic acid transporters), Member 2 (putative transporter) (SLC16A2, Accession NM\_006517) is another VGAM1958 host target gene. SLC16A2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC16A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC16A2 BINDING SITE, designated SEQ ID:13270, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66671] Another function of VGAM1958 is therefore inhibition of Solute Carrier Family 16 (monocarboxylic acid transporters), Member 2 (putative transporter) (SLC16A2, Accession NM\_006517). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC16A2. Solute Carrier Family 18 (vesicular monoamine), Member 1 (SLC18A1, Accession NM\_003053) is another VGAM1958 host target gene. SLC18A1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC18A1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC18A1 BINDING SITE, designated SEQ ID:9015, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66672] Another function of VGAM1958 is therefore inhibition of Solute Carrier Family 18 (vesicular monoamine), Member 1 (SLC18A1, Accession NM\_003053), a gene which is involved in the vesicular transport of biogenic amines. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC18A1. The function of SLC18A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18. Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM\_003038) is another VGAM1958 host target gene. SLC1A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of SLC1A4 BINDING SITE, designated SEQ ID:8995, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66673] Another function of VGAM1958 is therefore inhibition of Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM\_003038), a gene which transports alanine, serine, cysteine, and threonine. exhibits sodium dependence. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A4. The function of SLC1A4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM859. Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM\_005628) is another VGAM1958 host target gene. SLC1A5 BINDING SITE1 and SLC1A5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC1A5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A5

BINDING SITE1 and SLC1A5 BINDING SITE2, designated SEQ ID:12143 and SEQ ID:38403 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66674] Another function of VGAM1958 is therefore inhibition of Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM\_005628). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A5. Solute Carrier Family 25 (mitochondrial carrier, brain), Member 14 (SLC25A14, Accession NM\_022810) is another VGAM1958 host target gene. SLC25A14 BINDING SITE1 and SLC25A14 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC25A14, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC25A14 BINDING SITE1 and SLC25A14 BINDING SITE2, designated SEQ ID:23086 and SEQ ID:10087 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66675] Another function of VGAM1958 is therefore inhibition of

Solute Carrier Family 25 (mitochondrial carrier, brain), Member 14 (SLC25A14, Accession NM\_022810), a gene which participates in the mitochondrial proton leak measured in brain mitochondria. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC25A14. The function of SLC25A14 has been established by previous studies. Uncoupling proteins (UCPs) are proton channel carrier proteins not coupled to oxidative phosphorylation. They are located in the inner membrane of mitochondria and have been linked to the generation of heat. UCP1 (OMIM Ref. No. 113730) is localized to brown adipose tissue, UCP2 (OMIM Ref. No. 601693) is widely expressed, and UCP3 (OMIM Ref. No. 602044) is largely found in skeletal muscle. By searching an EST database for UCPs and screening a brain cDNA library, Sanchis et al. (1998) obtained a cDNA encoding SLC25A14, which they called 'brain mitochondrial carrier protein-1,' or BMCP1. The deduced 325-amino acid SLC25A14 protein contains 6 transmembrane domains, 3 motifs characteristic of mitochondrial energy transfer proteins, and 20 amino acids at the N terminus that are absent in UCP1, UCP2, and UCP3. SLC25A14 shares 34, 38, and 39% amino acid iden-

tity with UCP1, UCP2, and UCP3, respectively. Northern blot analysis detected high expression of a 1.8-kb SLC25A14 transcript in brain. RNA dot-blot analysis detected SLC25A14 expression in testis and pituitary. In situ hybridization analysis in mouse brain showed Slc25a14 expression in hypothalamus, cortex, hippocampus, thalamus, and amygdala. Functional analysis in yeast showed that SLC25A14 expression correlates with impaired growth rate and a marked uncoupling of respiration, suggesting that SLC25A14 may be a member of the UCP family Sanchis et al. (1998) identified an STS (GenBank G23624) mapping to Xq24 within the SLC25A14 gene. By analysis of a backcross panel, they mapped the mouse Slc25a14 gene to the X chromosome as well

[66676] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66677] Sanchis, D.; Fleury, C.; Chomiki, N.; Goubern, M.; Huang, Q.; Neverova, M.; Gregoire, F.; Easlick, J.; Raimbault, S.; Levi-Meyrueis, C.; Miroux, B.; Collins, S.; Seldin, M.; Richard, D.; Warden, C.; Bouillaud, F.; Ricquier, D. : BMCP1, a novel mitochondrial carrier with high expression in the central nervous system of humans and rodents, and

respiration uncoupling activity in recombinant yeast. J.

Biol. Chem. 273: 34611–34615, 1998. ; and

[66678] Sanchis, D.; Fleury, C.; Chomiki, N.; Goubern, M.; Huang, Q.; Neverova, M.; Gregoire, F.; Easlick, J.; Raimbault, S.; Levi-Meyrueis, C.; Miroux, B.; Collins, S.; Seldin, M.; Richard, D.; Wa.

[66679] Further studies establishing the function and utilities of SLC25A14 are found in John Hopkins OMIM database record ID 300242, and in cited publications numbered 9160 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 29 (nucleoside transporters), Member 1 (SLC29A1, Accession NM\_004955) is another VGAM1958 host target gene. SLC29A1 BINDING SITE1 and SLC29A1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC29A1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC29A1 BINDING SITE1 and SLC29A1 BINDING SITE2, designated SEQ ID:11400 and SEQ ID:19976 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66680] Another function of VGAM1958 is therefore inhibition of Solute Carrier Family 29 (nucleoside transporters), Member 1 (SLC29A1, Accession NM\_004955), a gene which mediates both influx and efflux of nucleosides across the membrane. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC29A1. The function of SLC29A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1908. Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 6 (SLC7A6, Accession NM\_003983) is another VGAM1958 host target gene. SLC7A6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC7A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A6 BINDING SITE, designated SEQ ID:10123, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66681] Another function of VGAM1958 is therefore inhibition of



Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 6 (SLC7A6, Accession NM\_003983), a gene which is involved in mediating amino acid transport. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A6. The function of SLC7A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM87. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily A, Member 5 (SMARCA5, Accession NM\_003601) is another VGAM1958 host target gene. SMARCA5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SMARCA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCA5 BINDING SITE, designated SEQ ID:9655, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66682] Another function of VGAM1958 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent

## Regulator of Chromatin, Subfamily A, Member 5

(SMARCA5, Accession NM\_003601), a gene which is involved in chromatin assembly and remodeling. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCA5. The function of SMARCA5 has been established by previous studies. Poot et al. (2000) identified SMARCA5, which they called SNF2H, within a chromatin remodeling complex, CHRAC, purified from HeLa cell nuclear extracts. They confirmed an interaction between SMARCA5 and ACF1 (BAZ1A). Two small histone-fold proteins, CHRAC17 (POLE3; 607267) and CHRAC15 (CHRAC1; 607268), copurified with the complex, and the authors showed that these proteins form a DNA-binding heterodimer. Poot et al. (2000) determined that the purified complex could mobilize nucleosomes into a regularly spaced nucleosomal array and that the spacing activity was strictly ATP-dependent. By Western blot analysis of protein expression levels in several human and mammalian cell lines, Bozhenok et al. (2002) determined that SMARCA5 interacts with BAZ1B (OMIM Ref. No. 605681). In vitro analysis of the mouse Smarca5-Baz1b complex showed that, in the presence of ATP, the complex can cre-

ate regular nucleosomal arrays from irregular chromatin

[66683] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66684] Bozhenok, L.; Wade, P. A.; Varga-Weisz, P. : WSTF-ISWI chromatin remodeling complex targets heterochromatic replication foci. EMBO J. 21: 2231–2241, 2002. ; and

[66685] Poot, R. A.; Dellaire, G.; Hulsmann, B. B.; Grimaldi, M. A.; Corona, D. F. V.; Becker, P. B.; Bickmore, W. A.; Varga-Weisz, P. D. : HuCHRAAC, a human ISWI chromatin remodeling complex cont.

[66686] Further studies establishing the function and utilities of SMARCA5 are found in John Hopkins OMIM database record ID 603375, and in cited publications numbered 5070–507 and 7226–5074 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1 (SMARCD1, Accession NM\_003076) is another VGAM1958 host target gene. SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMARCD1, corresponding to HOST TARGET binding sites such as BIND–

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2, designated SEQ ID:9043 and SEQ ID:29141 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66687] Another function of VGAM1958 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1 (SMARCD1, Accession NM\_003076), a gene which is involved in chromatin assembly and remodeling. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCD1. The function of SMARCD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152.SNL (Accession NM\_003088) is another VGAM1958 host target gene. SNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

SNL BINDING SITE, designated SEQ ID:9065, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66688] Another function of VGAM1958 is therefore inhibition of SNL (Accession NM\_003088), a gene which organizes filamentous actin into bundles with a minimum of 4.1:1 actin/fascin ratio. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNL. The function of SNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675.Sparc/osteonectin, Cwcv and Kazal-like Domains Proteoglycan (testican) (SPOCK, Accession XM\_031696) is another VGAM1958 host target gene. SPOCK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPOCK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPOCK BINDING SITE, designated SEQ ID:31458, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ

ID:4669.

[66689] Another function of VGAM1958 is therefore inhibition of Sparc/osteonectin, Cwcv and Kazal-like Domains Proteoglycan (testican) (SPOCK, Accession XM\_031696). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPOCK. Sequestosome 1 (SQSTM1, Accession NM\_003900) is another VGAM1958 host target gene. SQSTM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SQSTM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SQSTM1 BINDING SITE, designated SEQ ID:9990, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66690] Another function of VGAM1958 is therefore inhibition of Sequestosome 1 (SQSTM1, Accession NM\_003900), a gene which binds SH2 domain of p56lck and ubiquitin, and it is associated with a serine/threonine kinase activity. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with SQSTM1. The function of SQSTM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM824.V-src Sarcoma (Schmidt-Ruppin A-2) Viral Oncogene Homolog (avian) (SRC, Accession NM\_005417) is another VGAM1958 host target gene. SRC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRC BINDING SITE, designated SEQ ID:11888, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66691] Another function of VGAM1958 is therefore inhibition of V-src Sarcoma (Schmidt-Ruppin A-2) Viral Oncogene Homolog (avian) (SRC, Accession NM\_005417), a gene which is a tyrosine kinase. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRC. The function of SRC and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM721. Signal Transducer and Activator of Transcription 6, Interleukin-4 Induced (STAT6, Accession NM\_003153) is another VGAM1958 host target gene. STAT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAT6 BINDING SITE, designated SEQ ID:9131, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66692] Another function of VGAM1958 is therefore inhibition of Signal Transducer and Activator of Transcription 6, Interleukin-4 Induced (STAT6, Accession NM\_003153), a gene which carries out a dual function: signal transduction and activation of transcription. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAT6. The function of STAT6 has been established by previous studies. By searching a database of expressed sequence tags (ESTs), Quelle et al. (1995) identified a number of expressed genes in the signal transducers and activators of



a transcription (STAT) family. Human and murine full-length cDNA clones were obtained and sequenced. The sequence of the human cDNA was identical to the sequence published by Hou et al. (1994) for the interleukin-4-induced transcription factor (called by them IL4 Stat), while the murine STAT6 amino acid and nucleotide sequences reported by Quelle et al. (1995) were 83% and 84% identical to the human sequences, respectively. Using STAT6-specific antiserum, Quelle et al. (1995) demonstrated that STAT6 is rapidly tyrosine phosphorylated following stimulation of appropriate cell lines with IL4 (OMIM Ref. No. 147780) or IL3 (OMIM Ref. No. 147740), but is not detectably phosphorylated following stimulation with IL2 (OMIM Ref. No. 147680), IL12 (OMIM Ref. No. 161560), or erythropoietin (OMIM Ref. No. 133170). In contrast, IL2, IL3, and erythropoietin induced the tyrosine phosphorylation of STAT5 (OMIM Ref. No. 601511), while IL12 uniquely induced the tyrosine phosphorylation of STAT4 (OMIM Ref. No. 600558). Inducible tyrosine phosphorylation of STAT6 required the membrane-distal region of the IL4 receptor alpha chain (OMIM Ref. No. 147781). They found that this region of the receptor is not required for cell growth, demonstrating that STAT6

tyrosine phosphorylation does not contribute to mitogenesis. Ghilardi et al. (1996) demonstrated that along with STAT3 (OMIM Ref. No. 102582) and STAT5, STAT6 is involved in signaling from the leptin receptor (OMIM Ref. No. 601007) and that this signaling is defective in the db/db mouse which carries a point mutation within the leptin receptor gene. Darnell (1996) reflected on STAT3, STAT5, and STAT6 as 'fat STATs,' i.e., the involvement of these 3 STATs, but not STAT1, STAT2, and STAT4, in the physiologic action of leptin (OMIM Ref. No. 164160) as described by Ghilardi et al. (1996).

[66693] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66694] Ghilardi, N.; Ziegler, S.; Wiestner, A.; Stoffel, R.; Heim, M. H.; Skoda, R. C. : Defective STAT signaling by the leptin receptor in diabetic mice. Proc. Nat. Acad. Sci. 93: 6231–6235, 1996. ; and

[66695] Quelle, F. W.; Shimoda, K.; Thierfelder, W.; Fischer, C.; Kim, A.; Ruben, S. M.; Cleveland, J. L.; Pierce, J. H.; Keegan, A. D.; Nelms, K.; Paul, W. E.; Ihle, J. N. : Cloning of murin.

[66696] Further studies establishing the function and utilities of

STAT6 are found in John Hopkins OMIM database record ID 601512, and in cited publications numbered 8096, 9451, 11335, 9452, 11336, 2772–277 and 10044 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Serine/threonine Kinase 10 (STK10, Accession NM\_005990) is another VGAM1958 host target gene. STK10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK10 BINDING SITE, designated SEQ ID:12613, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66697] Another function of VGAM1958 is therefore inhibition of Serine/threonine Kinase 10 (STK10, Accession NM\_005990), a gene which can act on substrates such as myelin basic protein and histone iia on serine and threonine residues. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK10. The function of STK10 has been established by previous studies. Ku-

ramochi et al. (1997) cloned the mouse gene *Stk10*, coding for a new serine/threonine kinase, designated LOK. Kuramochi et al. (1999) described the cloning of a cDNA encoding the human homolog and the detection of LOK proteins in human lymphoid cells. They deposited the sequence of a human LOK cDNA in GenBank (AB015718). They also determined the chromosomal location of the gene by fluorescence in situ hybridization: 5q35.1 in human, 11A4 in mouse, and 10q12.3 in rat. By means of polymorphic CA repeats found in the 3-prime untranslated region of the mouse *Stk10* gene and an intersubspecific backcross mapping panel, they mapped the *Stk10* locus to a restricted region on chromosome 11 between D11Mit53 and D11Mit84. These results established STK10 as a new marker of human chromosome 5 to define the syntenic boundary of human chromosomes 5 and 16 on mouse chromosome 11.

[66698] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66699] Kuramochi, S.; Matsuda, Y.; Okamoto, M.; Kitamura, F.; Yonekawa, H.; Karasuyama, H. : Molecular cloning of the human gene STK10 encoding lymphocyte-oriented kinase,

and comparative chromosomal mapping of the human, mouse, and rat homologues. Immunogenetics 49: 369–375, 1999. ; and

[66700] Kuramochi, S.; Moriguchi, T.; Kuida, K.; Endo, J.; Semba, K.; Nishida, E.; Karasuyama, H. : LOK is a novel mouse STE20–like protein kinase that is expressed predominantly in lymphocyte.

[66701] Further studies establishing the function and utilities of STK10 are found in John Hopkins OMIM database record ID 603919, and in cited publications numbered 1005–1006 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Serine/threonine Kinase 11 (Peutz–Jeghers syndrome) (STK11, Accession NM\_000455) is another VGAM1958 host target gene. STK11 BINDING SITE1 and STK11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by STK11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK11 BINDING SITE1 and STK11 BINDING SITE2, designated SEQ ID:6069 and SEQ ID:6070 respectively, to the nucleotide sequence of VGAM1958 RNA,

herein designated VGAM RNA, also designated SEQ ID:4669.

[66702] Another function of VGAM1958 is therefore inhibition of Serine/threonine Kinase 11 (Peutz–Jeghers syndrome) (STK11, Accession NM\_000455). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK11. Surfeit 4 (SURF4, Accession NM\_033161) is another VGAM1958 host target gene. SURF4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SURF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SURF4 BINDING SITE, designated SEQ ID:27012, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66703] Another function of VGAM1958 is therefore inhibition of Surfeit 4 (SURF4, Accession NM\_033161), a gene which is a conserved integral membrane protein containing multiple putative transmembrane regions. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

SURF4. The function of SURF4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM496.SWAP70 (Accession XM\_049197) is another VGAM1958 host target gene. SWAP70 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SWAP70, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SWAP70 BINDING SITE, designated SEQ ID:35347, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66704] Another function of VGAM1958 is therefore inhibition of SWAP70 (Accession XM\_049197), a gene which is involved not only in nuclear events but also in signaling in B-cell activation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SWAP70. The function of SWAP70 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1090.Synaptogyrin 1 (SYNGR1, Accession

NM\_004711) is another VGAM1958 host target gene. SYNGR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNGR1 BINDING SITE, designated SEQ ID:11066, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66705] Another function of VGAM1958 is therefore inhibition of Synaptogyrin 1 (SYNGR1, Accession NM\_004711), a gene which belongs to transmembrane synaptic vesicle protein and may function in membrane recycling. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR1. The function of SYNGR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. Synaptogyrin 3 (SYNGR3, Accession NM\_004209) is another VGAM1958 host target gene. SYNGR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by



SYNGR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNGR3 BINDING SITE, designated SEQ ID:10405, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66706] Another function of VGAM1958 is therefore inhibition of Synaptogyrin 3 (SYNGR3, Accession NM\_004209). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR3. TATA Box Binding Protein (TBP)-associated Factor, RNA Polymerase I, C, 110kDa (TAF1C, Accession NM\_005679) is another VGAM1958 host target gene. TAF1C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TAF1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF1C BINDING SITE, designated SEQ ID:12236, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66707] Another function of VGAM1958 is therefore inhibition of TATA Box Binding Protein (TBP)–associated Factor, RNA Polymerase I, C, 110kDa (TAF1C, Accession NM\_005679), a gene which belongs to component of the RNA polymerase I and II SL1 transcription factor. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF1C. The function of TAF1C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. T-cell Acute Lymphocytic Leukemia 1 (TAL1, Accession NM\_003189) is another VGAM1958 host target gene. TAL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAL1 BINDING SITE, designated SEQ ID:9175, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66708] Another function of VGAM1958 is therefore inhibition of T-cell Acute Lymphocytic Leukemia 1 (TAL1, Accession

NM\_003189), a gene which may help control cell growth and differentiation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAL1. The function of TAL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Tafazzin (cardiomyopathy, dilated 3A (X-linked); Endocardial Fibroelastosis 2; Barth Syndrome) (TAZ, Accession NM\_000116) is another VGAM1958 host target gene. TAZ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAZ BINDING SITE, designated SEQ ID:5586, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66709] Another function of VGAM1958 is therefore inhibition of Tafazzin (cardiomyopathy, dilated 3A (X-linked); Endocardial Fibroelastosis 2; Barth Syndrome) (TAZ, Accession NM\_000116). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with TAZ. Transducin (beta)-like 1X-linked (TBL1X, Accession NM\_005647) is another VGAM1958 host target gene. TBL1X BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TBL1X, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBL1X BINDING SITE, designated SEQ ID:12187, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66710] Another function of VGAM1958 is therefore inhibition of Transducin (beta)-like 1X-linked (TBL1X, Accession NM\_005647), a gene which activates latent HDAC3 activity. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBL1X. The function of TBL1X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1151. Transducin (beta)-like 2 (TBL2, Accession NM\_032988) is another VGAM1958 host target gene. TBL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by TBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBL2 BINDING SITE, designated SEQ ID:26868, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66711] Another function of VGAM1958 is therefore inhibition of Transducin (beta)-like 2 (TBL2, Accession NM\_032988), a gene which is of unknown function. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBL2. The function of TBL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229. TATA Box Binding Protein (TBP, Accession XM\_035700) is another VGAM1958 host target gene. TBP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBP BINDING SITE, designated SEQ ID:32330, to the nu-

cleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66712] Another function of VGAM1958 is therefore inhibition of TATA Box Binding Protein (TBP, Accession XM\_035700), a gene which plays a central role in the initiation of eukaryotic mRNA synthesis. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBP. The function of TBP has been established by previous studies. The TBP C-terminal domain of 180 amino acids is well conserved, and this domain is both necessary and sufficient for interaction with DNA and for assembly of the basal transcription apparatus (Peterson et al., 1990). Contrary to the previously hypothesized existence of a family of genes coding for DNA-binding proteins highly related to TBP, Purrello et al. (1994) showed that the segment coding for the evolutionarily conserved C-terminal DNA-binding domain is unique. When bound to the TATA box, it has a saddle-like shape, with the concave face contacting DNA and the convex interacting with the other subunits of TFIID, which are called TBP-associated factors (TAFs; OMIM Ref. No. 600475), with TFIIA (600519, 600520) and TFIIB (OMIM Ref. No. 189963), with the A form of RNA

polymerase II CTD, and with positive and negative modulators of basal and activated transcription of class II genes (reviewed by Nikolov et al., 1992). The N terminus of TBP modulates the DNA-binding activity of the C terminus of the protein. It contains a long string of glutamine codons, which represents a common motif among other proteins involved in transcription, such as SP1 (OMIM Ref. No. 189906) and some homeo box proteins (Purrello et al., 1994). Animal model experiments lend further support to the function of TBP. Veenstra et al. (2000) tested the role of Tbp during the onset of embryonic transcription in *Xenopus* by antisense oligonucleotide-mediated turnover of maternal Tbp mRNA. Embryos without detectable Tbp initiated gastrulation but died before completing gastrulation. The expression of many genes transcribed by RNA polymerase II and III was reduced; however, some genes were transcribed with an efficiency identical to that of Tbp-containing embryos. Using a similar antisense strategy, Veenstra et al. (2000) found that the TBP-like factor Tlf/Trf2 (TBPL1; 605521) was essential for development past the midblastula stage. Because TBP and a TLF factor were found to play complementary roles in embryonic development, Veenstra et al. (2000) concluded that their re-

sults indicate that although similar mechanistic roles exist in common, TBP and TLF function differentially to control transcription of specific genes.

[66713] It is appreciated that the abovementioned animal model for TBP is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[66714] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66715] Purrello, M.; Pietro, C. D.; Mirabile, E.; Rapisarda, A.; Rimini, R.; Tine, A.; Pavone, L.; Motta, S.; Grzeschik, K.-H.; Sichel, G. : Physical mapping at 6q27 of the locus for the TATA box-binding protein, the DNA-binding subunit of TFIID and a component of SL1 and TFIIB, strongly suggests that it is single copy in the human genome. *Genomics* 22: 94–100, 1994. ; and

[66716] Veenstra, G. J. C.; Weeks, D. L.; Wolffe, A. P. : Distinct roles for TBP and TBP-like factor in early embryonic gene transcription in *Xenopus*. *Science* 290: 2312–2314, 2000.

[66717] Further studies establishing the function and utilities of TBP are found in John Hopkins OMIM database record ID 600075, and in cited publications numbered 7663–7672,



7678–7675, 788 and 7895–7896 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tec Protein Tyrosine Kinase (TEC, Accession NM\_003215) is another VGAM1958 host target gene. TEC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEC BINDING SITE, designated SEQ ID:9217, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66718] Another function of VGAM1958 is therefore inhibition of Tec Protein Tyrosine Kinase (TEC, Accession NM\_003215). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEC. Testis Derived Transcript (3 LIM domains) (TES, Accession XM\_050430) is another VGAM1958 host target gene. TES BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TES, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of TES BINDING SITE, designated SEQ ID:35630, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66719] Another function of VGAM1958 is therefore inhibition of Testis Derived Transcript (3 LIM domains) (TES, Accession XM\_050430), a gene which acts as a tumor suppressor. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TES. The function of TES and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM363. Testis-specific Kinase 1 (TESK1, Accession NM\_006285) is another VGAM1958 host target gene. TESK1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TESK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TESK1 BINDING SITE, designated SEQ ID:12971, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66720] Another function of VGAM1958 is therefore inhibition of Testis-specific Kinase 1 (TESK1, Accession NM\_006285), a gene which plays a central role at, and after the meiotic phase of spermatogenesis. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSK1. The function of TSK1 has been established by previous studies. Toshima et al. (1995) isolated cDNA clones encoding the rat and human forms of testis-specific protein kinase-1 (TESK1). The deduced 626-amino acid human protein shares 92% sequence identity with its rat counterpart. The protein kinase domain is structurally similar to those of LIMK1 (OMIM Ref. No. 601329) and LIMK2 (OMIM Ref. No. 601988), with 49 to 50% sequence identity. Studying transgenic mice carrying a lacZ reporter plasmid for TSK1 expression, Toshima et al. (2001) found TSK1 in testicular germ cells only in postpubertal mice at the pachytene spermatocyte to sperm stage of maturation. No staining was detected in nongerminal cells or in germ cells at other stages. Expression was also found in adult renal proximal convoluted tubules, in cardiac myocytes, in pulmonary smooth muscle cells around bronchioles, and within neurons of several areas of the adult brain. Intense

staining was also found in brain, spinal cord, and olfactory region of day 12.5 embryonic mice.

[66721] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66722] Toshima, J.; Ohashi, K.; Okano, I.; Nunoue, K.; Kishioka, M.; Kuma, K.; Miyata, T.; Hirai, M.; Baba, T.; Mizuno, K. : Identification and characterization of a novel protein kinase, TESK1, specifically expressed in testicular germ cells. *J. Biol. Chem.* 270: 31331–31337, 1995. ; and

[66723] Toshima, J.; Toshima, J. Y.; Suzuki, M.; Noda, T.; Mizuno, K. : Cell-type-specific expression of a TESK1 promoter-linked lacZ gene in transgenic mice. *Biochem. Biophys. Res. Commun.* 286:.

[66724] Further studies establishing the function and utilities of TESK1 are found in John Hopkins OMIM database record ID 601782, and in cited publications numbered 1249–1250 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcription Factor EB (TFEB, Accession XM\_166390) is another VGAM1958 host target gene. TFEB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TFEB, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFEB BINDING SITE, designated SEQ ID:44240, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66725] Another function of VGAM1958 is therefore inhibition of Transcription Factor EB (TFEB, Accession XM\_166390), a gene which may function as a transcription factor. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFEB. The function of TFEB has been established by previous studies. Transcription factors of the basic helix-loop-helix zipper (bHLH-Zip) family contain a basic domain, used for DNA binding, and HLH and Zip domains, both used for oligomerization. TFEB was isolated from a human B-cell cDNA library using a binding sequence from the adenovirus major late promoter (Carr and Sharp, 1990). By interspecific backcross analysis, Steingrimsen et al. (1995) mapped the Tcfef gene in the mouse to chromosome 17 in a region of homology to human 6p21, which can be presumed to be the location of the human homolog.

[66726] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66727] Carr, C. S.; Sharp, P. A. : A helix-loop-helix protein related to the immunoglobulin E box-binding proteins. Molec. Cell. Biol. 10: 4384-4388, 1990. ; and

[66728] Steingrimsson, E.; Sawadogo, M.; Gilbert, D. J.; Zervos, A. S.; Brent, R.; Blonar, M. A.; Fisher, D. E.; Copeland, N. G.; Jenkins, N. A. : Murine chromosomal location of five bHLH-Zip t.

[66729] Further studies establishing the function and utilities of TFEB are found in John Hopkins OMIM database record ID 600744, and in cited publications numbered 758 and 12617 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transforming Growth Factor, Beta 3 (TGFB3, Accession NM\_003239) is another VGAM1958 host target gene. TGFB3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TGFB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB3 BINDING SITE, designated SEQ ID:9232,

to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66730] Another function of VGAM1958 is therefore inhibition of Transforming Growth Factor, Beta 3 (TGFB3, Accession NM\_003239), a gene which is involved in embryogenesis and cell differentiation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB3. The function of TGFB3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1126. Translocase of Inner Mitochondrial Membrane 23 Homolog (yeast) (TIMM23, Accession XM\_011891) is another VGAM1958 host target gene. TIMM23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIMM23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIMM23 BINDING SITE, designated SEQ ID:30200, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66731] Another function of VGAM1958 is therefore inhibition of Translocase of Inner Mitochondrial Membrane 23 Homolog (yeast) (TIMM23, Accession XM\_011891), a gene which translocates nuclear-encoded proteins into the mitochondrion. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIMM23. The function of TIMM23 has been established by previous studies. By searching EST databases for homologs of yeast TIMs, Bauer et al. (1999) identified a cDNA encoding TIMM23. Sequence analysis predicted that the 209-amino acid TIMM23 protein shares 22% amino acid identity with yeast Tim23 and contains 4 hydrophobic membrane-spanning segments that conserve the N-out/C-out topology of yeast TIMs. TIMM23 also has a 74-amino acid N-terminal hydrophilic segment that is dissimilar to the N-terminal hydrophilic domain of yeast Tim23. Northern blot analysis detected a 2.9-kb TIMM23 transcript that was highly expressed in heart and skeletal muscle, intermediately expressed in brain, and weakly expressed in pancreas, placenta, kidney, and liver. Western blot analysis showed that TIMM23 colocalizes with the inner membrane fraction of mitochondria as a 23-kD protein. TIMM23 is organized



into 2 distinct 110-kD complexes in the inner membrane, one containing TIMM17A (OMIM Ref. No. 605057) and the other containing TIMM17B (OMIM Ref. No. 300249).

Tim23, a key component of the yeast mitochondrial pre-protein translocase, is anchored in the inner membrane by its C-terminal domain and exposes an intermediate domain, which functions as a presequence receptor, in the intermembrane space. Donzeau et al. (2000) showed that the N-terminal domain of Tim23 is exposed on the surface of the outer membrane. The authors stated that the 2-membrane-spanning topology of Tim23 is a novel characteristic in membrane biology. By simultaneously integrating into 2 membranes, Tim23 forms contacts between the outer and inner mitochondrial membranes. Tethering the inner membrane translocase to the outer membrane facilitates the transfer of precursor proteins from the TOM complex to the TIM23 complex, thereby increasing the efficiency of protein import.

[66732] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66733] Bauer, M. F.; Gempel, K.; Reichert, A. S.; Rappold, G. A.; Lichtner, P.; Gerbitz, K.-D.; Neupert, W.; Brunner, M.; Hof-

mann, S. : Genetic and structural characterization of the human mitochondrial inner membrane translocase. J. Molec. Biol. 289: 69–82, 1999. ; and

[66734] Donzeau, M.; Kaldi, K.; Adam, A.; Paschen, S.; Wanner, G.; Guiard, B.; Bauer, M. F.; Neupert, W.; Brunner, M. : Tim23 links the inner and outer mitochondrial membranes. Cell 101: 401–.

[66735] Further studies establishing the function and utilities of TIMM23 are found in John Hopkins OMIM database record ID 605034, and in cited publications numbered 9210 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TIRAP (Accession NM\_052887) is another VGAM1958 host target gene. TIRAP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TIRAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIRAP BINDING SITE, designated SEQ ID:27472, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66736] Another function of VGAM1958 is therefore inhibition of TIRAP (Accession NM\_052887), a gene which is a adapter

involved in the TLR4 signaling pathway in the innate immune response. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIRAP. The function of TIRAP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM189. Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM\_003257) is another VGAM1958 host target gene. TJP1 BINDING SITE1 and TJP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TJP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TJP1 BINDING SITE1 and TJP1 BINDING SITE2, designated SEQ ID:9266 and SEQ ID:9264 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66737] Another function of VGAM1958 is therefore inhibition of Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM\_003257), a gene which colocalizes and interacts with cadherins in cells lacking tight junctions. Accord-

ingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TJP1. The function of TJP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. T-cell Leukemia, Homeobox 1 (TLX1, Accession NM\_005521) is another VGAM1958 host target gene. TLX1 BINDING SITE1 and TLX1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TLX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLX1 BINDING SITE1 and TLX1 BINDING SITE2, designated SEQ ID:12045 and SEQ ID:30009 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66738] Another function of VGAM1958 is therefore inhibition of T-cell Leukemia, Homeobox 1 (TLX1, Accession NM\_005521), a gene which controls the spleen development. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLX1. The function of TLX1 and its

association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1505. Tumor Necrosis Factor (ligand) Superfamily, Member 15 (TNFSF15, Accession NM\_005118) is another VGAM1958 host target gene. TNFSF15 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TNFSF15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF15 BINDING SITE, designated SEQ ID:11599, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66739] Another function of VGAM1958 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 15 (TNFSF15, Accession NM\_005118), a gene which acts as an autocrine factor to induce apoptosis in endothelial cells. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFSF15. The function of TNFSF15 and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM350. Topoisomerase (DNA) III Alpha (TOP3A, Accession NM\_004618) is another VGAM1958 host target gene. TOP3A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TOP3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOP3A BINDING SITE, designated SEQ ID:10961, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66740] Another function of VGAM1958 is therefore inhibition of Topoisomerase (DNA) III Alpha (TOP3A, Accession NM\_004618). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOP3A. Translocated Promoter Region (to activated MET oncogene) (TPR, Accession NM\_003292) is another VGAM1958 host target gene. TPR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TPR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of TPR BINDING SITE, designated SEQ ID:9302, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66741] Another function of VGAM1958 is therefore inhibition of Translocated Promoter Region (to activated MET oncogene) (TPR, Accession NM\_003292), a gene which Large coiled coil protein; may be involved in nuclear protein import. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPR. The function of TPR has been established by previous studies. The TPR locus, which has been mapped to chromosome 1, expresses a 10-kb RNA in all human cell lines tested (Dean et al., 1985). In a cell line rendered tumorigenic with the direct-acting carcinogen N-methyl-N-prime-nitronitrosoguanidine (MNNG), Dean et al. (1987) defined an activated MET oncogene that expresses a novel 5.0-kb RNA transcript which is a hybrid RNA derived from a DNA rearrangement involving the TPR locus and the MET locus (on 7q; 164860). Although most of the hybrid RNA is derived from the MET oncogene, the 5-prime portion uses some exons from the TPR gene, presumably the promoter region. Oncogenic activation of

MET is reminiscent of the Philadelphia chromosomal translocation in chronic myeloid leukemia that generates the hybrid BCR/ABL tyrosine kinase p210 (see OMIM Ref. No. 151410). Gonzatti-Haces et al. (1988) identified the proteins encoded by the human TPR-MET oncogene and the human MET protooncogene. By fluorescence in situ hybridization, Miranda et al. (1994) assigned the TPR gene to 1q25.

[66742] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[66743] Dean, M.; Park, M.; Vande Woude, G. F. : Characterization of the rearranged TPR-MET oncogene breakpoint. *Molec. Cell. Biol.* 7: 921-924, 1987. ; and

[66744] Gonzatti-Haces, M.; Seth, A.; Park, M.; Copeland, T.; Oroszlan, S.; Vande Woude, G. F. : Characterization of the TPR-MET oncogene p65 and the MET protooncogene p140 protein-tyrosine kina.

[66745] Further studies establishing the function and utilities of TPR are found in John Hopkins OMIM database record ID 189940, and in cited publications numbered 182 and 12345-602 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tripartite



Motif-containing 14 (TRIM14, Accession NM\_014788) is another VGAM1958 host target gene. TRIM14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM14 BINDING SITE, designated SEQ ID:16666, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66746] Another function of VGAM1958 is therefore inhibition of Tripartite Motif-containing 14 (TRIM14, Accession NM\_014788), a gene which is composed of 3 zinc-binding domains and is involved in development and cell growth. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM14. The function of TRIM14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM\_004621) is another VGAM1958 host target gene. TRPC6 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by TRPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC6 BINDING SITE, designated SEQ ID:10972, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66747] Another function of VGAM1958 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM\_004621), a gene which has calcium channel activity. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC6. The function of TRPC6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Tuftelin 1 (TUFT1, Accession NM\_020127) is another VGAM1958 host target gene. TUFT1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TUFT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of TUFT1 BINDING SITE, designated SEQ ID:21317, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66748] Another function of VGAM1958 is therefore inhibition of Tuftelin 1 (TUFT1, Accession NM\_020127), a gene which appears to play a role in cytokinesis, cell shape, and specialized functions such as secretion and capping. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUFT1. The function of TUFT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1152. Twist Homolog (acrocephalosyndactyly 3; Saethre-Chotzen syndrome) (Drosophila) (TWIST, Accession NM\_000474) is another VGAM1958 host target gene. TWIST BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TWIST, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TWIST BINDING SITE, designated SEQ ID:6083, to the nucleotide sequence of

VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66749] Another function of VGAM1958 is therefore inhibition of Twist Homolog (acrocephalosyndactyly 3; Saethre-Chotzen syndrome) (*Drosophila*) (TWIST, Accession NM\_000474). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TWIST. Unc-119 Homolog (*C. elegans*) (UNC119, Accession NM\_054035) is another VGAM1958 host target gene. UNC119 BINDING SITE1 and UNC119 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UNC119, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UNC119 BINDING SITE1 and UNC119 BINDING SITE2, designated SEQ ID:27648 and SEQ ID:11621 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66750] Another function of VGAM1958 is therefore inhibition of Unc-119 Homolog (*C. elegans*) (UNC119, Accession NM\_054035), a gene which is expressed in the retina and

may play a role in the mechanism of photoreceptor neurotransmitter release through the synaptic vesicle cycle. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNC119. The function of UNC119 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1044.

Williams–Beuren Syndrome Chromosome Region 1 (WBSCR1, Accession NM\_031992) is another VGAM1958 host target gene. WBSCR1 BINDING SITE1 and WBSCR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WBSCR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WBSCR1 BINDING SITE1 and WBSCR1 BINDING SITE2, designated SEQ ID:25706 and SEQ ID:9649 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66751] Another function of VGAM1958 is therefore inhibition of Williams–Beuren Syndrome Chromosome Region 1

(WBSCR1, Accession NM\_031992), a gene which stimulates protein translation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WBSCR1. The function of WBSCR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM110. Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM\_014919) is another VGAM1958 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE5, designated SEQ ID:17182, SEQ ID:28463, SEQ ID:28474, SEQ ID:28446 and SEQ ID:10996 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66752] Another function of VGAM1958 is therefore inhibition of Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Acces-

sion NM\_014919), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 3 (XRCC3, Accession NM\_005432) is another VGAM1958 host target gene. XRCC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XRCC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XRCC3 BINDING SITE, designated SEQ ID:11908, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66753] Another function of VGAM1958 is therefore inhibition of X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 3 (XRCC3, Accession NM\_005432), a gene which is required for meiotic recombination, synapto-

mal complex formation and cell cycle progression. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XRCC3. The function of XRCC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1290. Zinc Finger Protein 103 Homolog (mouse) (ZFP103, Accession NM\_005667) is another VGAM1958 host target gene. ZFP103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZFP103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP103 BINDING SITE, designated SEQ ID:12218, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66754] Another function of VGAM1958 is therefore inhibition of Zinc Finger Protein 103 Homolog (mouse) (ZFP103, Accession NM\_005667). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP103. Zinc Finger Protein 136 (clone pHZ-20) (ZNF136, Accession



XM\_009075) is another VGAM1958 host target gene.

ZNF136 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF136 BINDING SITE, designated SEQ ID:30098, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66755] Another function of VGAM1958 is therefore inhibition of Zinc Finger Protein 136 (clone pHZ-20) (ZNF136, Accession XM\_009075). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF136. Zinc Finger Protein 215 (ZNF215, Accession NM\_013250) is another VGAM1958 host target gene. ZNF215 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF215 BINDING SITE, designated SEQ ID:14914, to the nucleotide

sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66756] Another function of VGAM1958 is therefore inhibition of Zinc Finger Protein 215 (ZNF215, Accession NM\_013250). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF215. Zinc Finger Protein 261 (ZNF261, Accession NM\_005096) is another VGAM1958 host target gene. ZNF261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF261 BINDING SITE, designated SEQ ID:11562, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66757] Another function of VGAM1958 is therefore inhibition of Zinc Finger Protein 261 (ZNF261, Accession NM\_005096). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF261. Zinc Finger Protein 278 (ZNF278, Accession NM\_032052) is another VGAM1958

host target gene. ZNF278 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF278, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF278 BINDING SITE, designated SEQ ID:25779, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66758] Another function of VGAM1958 is therefore inhibition of Zinc Finger Protein 278 (ZNF278, Accession NM\_032052), a gene which represses basal transcription as well as RNF4-mediated activation. Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF278. The function of ZNF278 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM414.A2BP1 (Accession NM\_018723) is another VGAM1958 host target gene. A2BP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by A2BP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of A2BP1 BINDING SITE, designated SEQ ID:20806, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66759] Another function of VGAM1958 is therefore inhibition of A2BP1 (Accession NM\_018723). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with A2BP1. ABIN-2 (Accession NM\_024309) is another VGAM1958 host target gene. ABIN-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABIN-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABIN-2 BINDING SITE, designated SEQ ID:23603, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66760] Another function of VGAM1958 is therefore inhibition of ABIN-2 (Accession NM\_024309). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABIN-2.

A Kinase (PRKA) Anchor Protein (gravin) 12 (AKAP12, Accession NM\_005100) is another VGAM1958 host target gene. AKAP12 BINDING SITE1 and AKAP12 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AKAP12, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP12 BINDING SITE1 and AKAP12 BINDING SITE2, designated SEQ ID:11571 and SEQ ID:29311 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66761] Another function of VGAM1958 is therefore inhibition of A Kinase (PRKA) Anchor Protein (gravin) 12 (AKAP12, Accession NM\_005100). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP12. AMSH (Accession NM\_006463) is another VGAM1958 host target gene. AMSH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMSH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of AMSH BINDING SITE, designated SEQ ID:13180, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66762] Another function of VGAM1958 is therefore inhibition of AMSH (Accession NM\_006463). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMSH. AND-1 (Accession NM\_007086) is another VGAM1958 host target gene. AND-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AND-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AND-1 BINDING SITE, designated SEQ ID:13955, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66763] Another function of VGAM1958 is therefore inhibition of AND-1 (Accession NM\_007086). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AND-1. Ankyrin Repeat Domain 5 (ANKRD5, Accession NM\_022096) is another VGAM1958 host target gene.

ANKRD5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ANKRD5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKRD5 BINDING SITE, designated SEQ ID:22635, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66764] Another function of VGAM1958 is therefore inhibition of Ankyrin Repeat Domain 5 (ANKRD5, Accession NM\_022096). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKRD5. Adaptor-related Protein Complex 3, Mu 2 Subunit (AP3M2, Accession NM\_006803) is another VGAM1958 host target gene. AP3M2 BINDING SITE1 and AP3M2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AP3M2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP3M2 BINDING SITE1 and AP3M2 BINDING SITE2, designated SEQ

ID:13674 and SEQ ID:13677 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66765] Another function of VGAM1958 is therefore inhibition of Adaptor-related Protein Complex 3, Mu 2 Subunit (AP3M2, Accession NM\_006803). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP3M2. APCL (Accession NM\_005883) is another VGAM1958 host target gene. APCL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APCL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APCL BINDING SITE, designated SEQ ID:12500, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66766] Another function of VGAM1958 is therefore inhibition of APCL (Accession NM\_005883). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APCL. APH2 (Accession NM\_032327) is another VGAM1958 host



target gene. APH2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by APH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APH2 BINDING SITE, designated SEQ ID:26135, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66767] Another function of VGAM1958 is therefore inhibition of APH2 (Accession NM\_032327). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APH2. ARHGAP11A (Accession NM\_014783) is another VGAM1958 host target gene. ARHGAP11A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ARHGAP11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP11A BINDING SITE, designated SEQ ID:16637, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66768] Another function of VGAM1958 is therefore inhibition of ARHGAP11A (Accession NM\_014783). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP11A. Rho Guanine Nucleotide Exchange Factor (GEF) 4 (ARHGEF4, Accession NM\_032995) is another VGAM1958 host target gene. ARHGEF4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARHGEF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF4 BINDING SITE, designated SEQ ID:26874, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66769] Another function of VGAM1958 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 4 (ARHGEF4, Accession NM\_032995). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF4. ARL8 (Accession XM\_167671) is another VGAM1958 host target gene. ARL8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by ARL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARL8 BINDING SITE, designated SEQ ID:44765, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66770] Another function of VGAM1958 is therefore inhibition of ARL8 (Accession XM\_167671). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARL8. ATPase, H<sup>+</sup> Transporting, Lysosomal V0 Subunit A Isoform 1 (ATP6V0A1, Accession NM\_005177) is another VGAM1958 host target gene. ATP6V0A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP6V0A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP6V0A1 BINDING SITE, designated SEQ ID:11676, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66771] Another function of VGAM1958 is therefore inhibition of

ATPase, H<sup>+</sup> Transporting, Lysosomal V0 Subunit A Iso-form 1 (ATP6V0A1, Accession NM\_005177). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP6V0A1. ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577) is another VGAM1958 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31077, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66772] Another function of VGAM1958 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. BANK (Accession NM\_017935) is another VGAM1958 host target gene. BANK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BANK,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BANK BINDING SITE, designated SEQ ID:19627, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66773] Another function of VGAM1958 is therefore inhibition of BANK (Accession NM\_017935). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BANK. BCMP1 (Accession NM\_031442) is another VGAM1958 host target gene. BCMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCMP1 BINDING SITE, designated SEQ ID:25459, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66774] Another function of VGAM1958 is therefore inhibition of BCMP1 (Accession NM\_031442). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with BCMP1. Baculoviral IAP Repeat-containing 1 (BIRC1, Accession NM\_004536) is another VGAM1958 host target gene. BIRC1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BIRC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIRC1 BINDING SITE, designated SEQ ID:10885, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66775] Another function of VGAM1958 is therefore inhibition of Baculoviral IAP Repeat-containing 1 (BIRC1, Accession NM\_004536). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC1. BM045 (Accession NM\_018459) is another VGAM1958 host target gene. BM045 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BM045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BM045 BINDING SITE, designated SEQ

ID:20531, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66776] Another function of VGAM1958 is therefore inhibition of BM045 (Accession NM\_018459). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BM045. BCL2/adenovirus E1B 19kDa Interacting Protein 2 (BNIP2, Accession XM\_039703) is another VGAM1958 host target gene. BNIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BNIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BNIP2 BINDING SITE, designated SEQ ID:33162, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66777] Another function of VGAM1958 is therefore inhibition of BCL2/adenovirus E1B 19kDa Interacting Protein 2 (BNIP2, Accession XM\_039703). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BNIP2. Blepharophimosis, Epicanthus Inversus and Ptosis, Candi-

date 1 (BPESC1, Accession NM\_021812) is another VGAM1958 host target gene. BPESC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BPESC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BPESC1 BINDING SITE, designated SEQ ID:22374, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66778] Another function of VGAM1958 is therefore inhibition of Blepharophimosis, Epicanthus Inversus and Ptosis, Candidate 1 (BPESC1, Accession NM\_021812). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BPESC1. Chromosome 11 Open Reading Frame 11 (C11orf11, Accession XM\_167769) is another VGAM1958 host target gene. C11orf11 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C11orf11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf11 BINDING SITE,



designated SEQ ID:44781, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66779] Another function of VGAM1958 is therefore inhibition of Chromosome 11 Open Reading Frame 11 (C11orf11, Accession XM\_167769). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf11. C16orf5 (Accession NM\_013399) is another VGAM1958 host target gene. C16orf5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C16orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C16orf5 BINDING SITE, designated SEQ ID:15057, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66780] Another function of VGAM1958 is therefore inhibition of C16orf5 (Accession NM\_013399). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C16orf5. Chromosome 1 Open Reading Frame 24

(C1orf24, Accession NM\_052966) is another VGAM1958 host target gene. C1orf24 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1orf24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf24 BINDING SITE, designated SEQ ID:27529, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66781] Another function of VGAM1958 is therefore inhibition of Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM\_052966). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf24. Chromosome 20 Open Reading Frame 103 (C20orf103, Accession NM\_012261) is another VGAM1958 host target gene. C20orf103 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf103 BINDING SITE, designated SEQ

ID:14571, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66782] Another function of VGAM1958 is therefore inhibition of Chromosome 20 Open Reading Frame 103 (C20orf103, Accession NM\_012261). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf103. Chromosome 20 Open Reading Frame 160 (C20orf160, Accession NM\_080625) is another VGAM1958 host target gene. C20orf160 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf160 BINDING SITE, designated SEQ ID:27932, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66783] Another function of VGAM1958 is therefore inhibition of Chromosome 20 Open Reading Frame 160 (C20orf160, Accession NM\_080625). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with C20orf160. Chromosome 20 Open Reading Frame 162 (C20orf162, Accession NM\_080603) is another VGAM1958 host target gene. C20orf162 BINDING SITE1 and C20orf162 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by C20orf162, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf162 BINDING SITE1 and C20orf162 BINDING SITE2, designated SEQ ID:27912 and SEQ ID:27917 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66784] Another function of VGAM1958 is therefore inhibition of Chromosome 20 Open Reading Frame 162 (C20orf162, Accession NM\_080603). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf162. Chromosome 20 Open Reading Frame 54 (C20orf54, Accession NM\_033409) is another VGAM1958 host target gene. C20orf54 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA

encoded by C20orf54, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf54 BINDING SITE, designated SEQ ID:27227, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66785] Another function of VGAM1958 is therefore inhibition of Chromosome 20 Open Reading Frame 54 (C20orf54, Accession NM\_033409). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf54. Chromosome 21 Open Reading Frame 18 (C21orf18, Accession NM\_017438) is another VGAM1958 host target gene. C21orf18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf18 BINDING SITE, designated SEQ ID:18897, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66786] Another function of VGAM1958 is therefore inhibition of Chromosome 21 Open Reading Frame 18 (C21orf18, Accession NM\_017438). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf18. C3IP1 (Accession NM\_021633) is another VGAM1958 host target gene. C3IP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C3IP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C3IP1 BINDING SITE, designated SEQ ID:22274, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66787] Another function of VGAM1958 is therefore inhibition of C3IP1 (Accession NM\_021633). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C3IP1. Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM\_032385) is another VGAM1958 host target gene. C5orf4 BINDING SITE1 and C5orf4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by C5orf4, corresponding to HOST

TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf4 BINDING SITE1 and C5orf4 BINDING SITE2, designated SEQ ID:26178 and SEQ ID:18473 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66788] Another function of VGAM1958 is therefore inhibition of Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM\_032385). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf4. Chromosome 7 Open Reading Frame 13 (C7orf13, Accession NM\_032625) is another VGAM1958 host target gene. C7orf13 BINDING SITE1 and C7orf13 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by C7orf13, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C7orf13 BINDING SITE1 and C7orf13 BINDING SITE2, designated SEQ ID:26342 and SEQ ID:39656 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ

ID:4669.

[66789] Another function of VGAM1958 is therefore inhibition of Chromosome 7 Open Reading Frame 13 (C7orf13, Accession NM\_032625). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C7orf13. Chromosome 9 Open Reading Frame 12 (C9orf12, Accession NM\_022755) is another VGAM1958 host target gene. C9orf12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C9orf12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf12 BINDING SITE, designated SEQ ID:22991, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66790] Another function of VGAM1958 is therefore inhibition of Chromosome 9 Open Reading Frame 12 (C9orf12, Accession NM\_022755). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf12. Chromosome 9 Open Reading Frame 7 (C9orf7, Accession NM\_017586)



is another VGAM1958 host target gene. C9orf7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C9orf7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf7 BINDING SITE, designated SEQ ID:19033, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66791] Another function of VGAM1958 is therefore inhibition of Chromosome 9 Open Reading Frame 7 (C9orf7, Accession NM\_017586). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf7. Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM\_018956) is another VGAM1958 host target gene. C9orf9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C9orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf9 BINDING SITE, designated SEQ ID:21024, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[66792] Another function of VGAM1958 is therefore inhibition of Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM\_018956). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf9. Calcium Channel, Voltage-dependent, Gamma Subunit 4 (CACNG4, Accession NM\_014405) is another VGAM1958 host target gene. CACNG4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CACNG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNG4 BINDING SITE, designated SEQ ID:15744, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66793] Another function of VGAM1958 is therefore inhibition of Calcium Channel, Voltage-dependent, Gamma Subunit 4 (CACNG4, Accession NM\_014405). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNG4. Calneuron 1 (CALN1, Accession NM\_031468) is

another VGAM1958 host target gene. CALN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25521, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66794] Another function of VGAM1958 is therefore inhibition of Calneuron 1 (CALN1, Accession NM\_031468). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. Calcium/calmodulin-dependent Protein Kinase Kinase 2, Beta (CAMKK2, Accession NM\_006549) is another VGAM1958 host target gene. CAMKK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK2 BINDING SITE, designated SEQ ID:13312, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[66795] Another function of VGAM1958 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 2, Beta (CAMKK2, Accession NM\_006549). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK2. Chromobox Homolog 1 (HP1 beta homolog *Drosophila*) (CBX1, Accession NM\_006807) is another VGAM1958 host target gene. CBX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CBX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBX1 BINDING SITE, designated SEQ ID:13680, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66796] Another function of VGAM1958 is therefore inhibition of Chromobox Homolog 1 (HP1 beta homolog *Drosophila*) (CBX1, Accession NM\_006807). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX1. Chromobox Homolog 6 (CBX6, Accession NM\_014292) is

another VGAM1958 host target gene. CBX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBX6 BINDING SITE, designated SEQ ID:15575, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66797] Another function of VGAM1958 is therefore inhibition of Chromobox Homolog 6 (CBX6, Accession NM\_014292). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX6. CD109 (Accession NM\_133493) is another VGAM1958 host target gene. CD109 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD109, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD109 BINDING SITE, designated SEQ ID:28569, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ

ID:4669.

[66798] Another function of VGAM1958 is therefore inhibition of CD109 (Accession NM\_133493). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD109. Cadherin-like 24 (CDH24, Accession XM\_170748) is another VGAM1958 host target gene. CDH24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH24 BINDING SITE, designated SEQ ID:45506, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66799] Another function of VGAM1958 is therefore inhibition of Cadherin-like 24 (CDH24, Accession XM\_170748). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH24. Cyclin-dependent Kinase-like 2 (CDC2-related kinase) (CDKL2, Accession NM\_003948) is another VGAM1958 host target gene. CDKL2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by CDKL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKL2 BINDING SITE, designated SEQ ID:10071, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66800] Another function of VGAM1958 is therefore inhibition of Cyclin-dependent Kinase-like 2 (CDC2-related kinase) (CDKL2, Accession NM\_003948). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKL2. Centaurin, Alpha 1 (CENTA1, Accession NM\_006869) is another VGAM1958 host target gene. CENTA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTA1 BINDING SITE, designated SEQ ID:13740, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66801] Another function of VGAM1958 is therefore inhibition of

Centaurin, Alpha 1 (CENTA1, Accession NM\_006869). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTA1. Centaurin, Gamma 1 (CENTG1, Accession NM\_014770) is another VGAM1958 host target gene. CENTG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTG1 BINDING SITE, designated SEQ ID:16567, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66802] Another function of VGAM1958 is therefore inhibition of Centaurin, Gamma 1 (CENTG1, Accession NM\_014770). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTG1. CG012 (Accession XM\_096710) is another VGAM1958 host target gene. CG012 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CG012, corresponding to a HOST TARGET binding site



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CG012 BINDING SITE, designated SEQ ID:40485, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66803] Another function of VGAM1958 is therefore inhibition of CG012 (Accession XM\_096710). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CG012. Chloride Intracellular Channel 4 (CLIC4, Accession NM\_013943) is another VGAM1958 host target gene. CLIC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLIC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIC4 BINDING SITE, designated SEQ ID:15132, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66804] Another function of VGAM1958 is therefore inhibition of Chloride Intracellular Channel 4 (CLIC4, Accession NM\_013943). Accordingly, utilities of VGAM1958 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIC4. Cyclin M4 (CNNM4, Accession NM\_020184) is another VGAM1958 host target gene. CNNM4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNNM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM4 BINDING SITE, designated SEQ ID:21427, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66805] Another function of VGAM1958 is therefore inhibition of Cyclin M4 (CNNM4, Accession NM\_020184). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM4. COP9 (Accession NM\_006710) is another VGAM1958 host target gene. COP9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by COP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COP9 BINDING SITE,

designated SEQ ID:13535, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66806] Another function of VGAM1958 is therefore inhibition of COP9 (Accession NM\_006710). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COP9. CPR2 (Accession NM\_030900) is another VGAM1958 host target gene. CPR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPR2 BINDING SITE, designated SEQ ID:25172, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66807] Another function of VGAM1958 is therefore inhibition of CPR2 (Accession NM\_030900). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPR2. Cysteine-rich with EGF-like Domains 1 (CRELD1, Accession NM\_015513) is another VGAM1958 host target gene.

CRELD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CRELD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRELD1 BINDING SITE, designated SEQ ID:17775, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66808] Another function of VGAM1958 is therefore inhibition of Cysteine-rich with EGF-like Domains 1 (CRELD1, Accession NM\_015513). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRELD1. CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM\_054838) is another VGAM1958 host target gene. CSMD1 BINDING SITE1 and CSMD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CSMD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSMD1 BINDING SITE1 and CSMD1 BINDING SITE2, designated SEQ ID:36193 and SEQ ID:27070 re-

spectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66809] Another function of VGAM1958 is therefore inhibition of CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM\_054838). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSMD1. DDM36 (Accession NM\_020962) is another VGAM1958 host target gene. DDM36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDM36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDM36 BINDING SITE, designated SEQ ID:21955, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66810] Another function of VGAM1958 is therefore inhibition of DDM36 (Accession NM\_020962). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDM36. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide

12 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX12, Accession XM\_006936) is another VGAM1958 host target gene. DDX12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX12 BINDING SITE, designated SEQ ID:30024, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66811] Another function of VGAM1958 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 12 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX12, Accession XM\_006936). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX12. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681) is another VGAM1958 host target gene. DDX34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE, designated SEQ ID:16164, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66812] Another function of VGAM1958 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. Diacylglycerol Kinase, Delta 130kDa (DGKD, Accession XM\_002384) is another VGAM1958 host target gene. DGKD BINDING SITE1 and DGKD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DGKD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKD BINDING SITE1 and DGKD BINDING SITE2, designated SEQ ID:29879 and SEQ ID:29884 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66813] Another function of VGAM1958 is therefore inhibition of

Diacylglycerol Kinase, Delta 130kDa (DGKD, Accession XM\_002384). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKD. Deiodinase, Iodothyronine, Type II (DIO2, Accession NM\_000793) is another VGAM1958 host target gene. DIO2 BINDING SITE1 and DIO2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DIO2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIO2 BINDING SITE1 and DIO2 BINDING SITE2, designated SEQ ID:6452 and SEQ ID:17300 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66814] Another function of VGAM1958 is therefore inhibition of Deiodinase, Iodothyronine, Type II (DIO2, Accession NM\_000793). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIO2. DKFZp434C0328 (Accession NM\_017577) is another VGAM1958 host target gene. DKFZp434C0328 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA



encoded by DKFZp434C0328, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434C0328 BINDING SITE, designated SEQ ID:19012, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66815] Another function of VGAM1958 is therefore inhibition of DKFZp434C0328 (Accession NM\_017577). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434C0328. DKFZP434C0826 (Accession XM\_097248) is another VGAM1958 host target gene. DKFZP434C0826 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434C0826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C0826 BINDING SITE, designated SEQ ID:40846, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66816] Another function of VGAM1958 is therefore inhibition of

DKFZP434C0826 (Accession XM\_097248). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C0826. DKFZP434C1715 (Accession XM\_098421) is another VGAM1958 host target gene. DKFZP434C1715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434C1715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C1715 BINDING SITE, designated SEQ ID:41674, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66817] Another function of VGAM1958 is therefore inhibition of DKFZP434C1715 (Accession XM\_098421). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C1715. DKFZP434E2135 (Accession NM\_030804) is another VGAM1958 host target gene. DKFZP434E2135 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434E2135, corresponding to a HOST TARGET bind-

ing site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434E2135 BINDING SITE, designated SEQ ID:25119, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66818] Another function of VGAM1958 is therefore inhibition of DKFZP434E2135 (Accession NM\_030804). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434E2135. DKFZp434F1719 (Accession NM\_032248) is another VGAM1958 host target gene. DKFZp434F1719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434F1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434F1719 BINDING SITE, designated SEQ ID:25986, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66819] Another function of VGAM1958 is therefore inhibition of DKFZp434F1719 (Accession NM\_032248). Accordingly,

utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434F1719. DKFZP434H204 (Accession XM\_039153) is another VGAM1958 host target gene. DKFZP434H204 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434H204, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434H204 BINDING SITE, designated SEQ ID:33015, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66820] Another function of VGAM1958 is therefore inhibition of DKFZP434H204 (Accession XM\_039153). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434H204. DKFZP434I216 (Accession XM\_085381) is another VGAM1958 host target gene. DKFZP434I216 BINDING SITE1 through DKFZP434I216 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZP434I216, corresponding to HOST TARGET binding sites such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I216 BINDING SITE1 through DKFZP434I216 BINDING SITE3, designated SEQ ID:38099, SEQ ID:38101 and SEQ ID:38102 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66821] Another function of VGAM1958 is therefore inhibition of DKFZP434I216 (Accession XM\_085381). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I216. DKFZP434K2235 (Accession XM\_096869) is another VGAM1958 host target gene. DKFZP434K2235 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434K2235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434K2235 BINDING SITE, designated SEQ ID:40595, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66822] Another function of VGAM1958 is therefore inhibition of

DKFZP434K2235 (Accession XM\_096869). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434K2235. DKFZp434O0320 (Accession XM\_097012) is another VGAM1958 host target gene. DKFZp434O0320 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434O0320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434O0320 BINDING SITE, designated SEQ ID:40706, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66823] Another function of VGAM1958 is therefore inhibition of DKFZp434O0320 (Accession XM\_097012). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434O0320. DKFZP434P0111 (Accession XM\_041116) is another VGAM1958 host target gene. DKFZP434P0111 BINDING SITE1 and DKFZP434P0111 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZP434P0111,

corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P0111 BINDING SITE1 and DKFZP434P0111 BINDING SITE2, designated SEQ ID:33457 and SEQ ID:33450 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66824] Another function of VGAM1958 is therefore inhibition of DKFZP434P0111 (Accession XM\_041116). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0111. DKFZP564O0463 (Accession NM\_014156) is another VGAM1958 host target gene. DKFZP564O0463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O0463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0463 BINDING SITE, designated SEQ ID:15445, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66825] Another function of VGAM1958 is therefore inhibition of DKFZP564O0463 (Accession NM\_014156). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0463. DKFZP566M1046 (Accession NM\_032127) is another VGAM1958 host target gene. DKFZP566M1046 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP566M1046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566M1046 BINDING SITE, designated SEQ ID:25812, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66826] Another function of VGAM1958 is therefore inhibition of DKFZP566M1046 (Accession NM\_032127). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566M1046. DKFZP586F1524 (Accession NM\_015584) is another VGAM1958 host target gene. DKFZP586F1524 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by



DKFZP586F1524, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586F1524 BINDING SITE, designated SEQ ID:17853, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66827] Another function of VGAM1958 is therefore inhibition of DKFZP586F1524 (Accession NM\_015584). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586F1524. DKFZP727C091 (Accession XM\_038689) is another VGAM1958 host target gene. DKFZP727C091 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP727C091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP727C091 BINDING SITE, designated SEQ ID:32906, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66828] Another function of VGAM1958 is therefore inhibition of

DKFZP727C091 (Accession XM\_038689). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP727C091. DKFZp761G2113 (Accession XM\_046017) is another VGAM1958 host target gene. DKFZp761G2113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761G2113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761G2113 BINDING SITE, designated SEQ ID:34644, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66829] Another function of VGAM1958 is therefore inhibition of DKFZp761G2113 (Accession XM\_046017). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761G2113. DKFZp761J139 (Accession NM\_032280) is another VGAM1958 host target gene. DKFZp761J139 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp761J139, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761J139 BINDING SITE, designated SEQ ID:26037, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66830] Another function of VGAM1958 is therefore inhibition of DKFZp761J139 (Accession NM\_032280). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761J139. DKFZp761K1423 (Accession NM\_018422) is another VGAM1958 host target gene. DKFZp761K1423 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp761K1423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761K1423 BINDING SITE, designated SEQ ID:20469, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66831] Another function of VGAM1958 is therefore inhibition of DKFZp761K1423 (Accession NM\_018422). Accordingly,

utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761K1423. DKFZp762K222 (Accession XM\_048721) is another VGAM1958 host target gene. DKFZp762K222 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp762K222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762K222 BINDING SITE, designated SEQ ID:35236, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66832] Another function of VGAM1958 is therefore inhibition of DKFZp762K222 (Accession XM\_048721). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762K222. DKFZp762P2111 (Accession XM\_098654) is another VGAM1958 host target gene. DKFZp762P2111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762P2111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762P2111 BINDING SITE, designated SEQ ID:41755, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66833] Another function of VGAM1958 is therefore inhibition of DKFZp762P2111 (Accession XM\_098654). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762P2111. Dystrophia Myotonica-containing WD Repeat Motif (DMWD, Accession XM\_027569) is another VGAM1958 host target gene. DMWD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DMWD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMWD BINDING SITE, designated SEQ ID:30532, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66834] Another function of VGAM1958 is therefore inhibition of Dystrophia Myotonica-containing WD Repeat Motif (DMWD, Accession XM\_027569). Accordingly, utilities of

VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMWD. DRIL2 (Accession NM\_006465) is another VGAM1958 host target gene. DRIL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DRIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRIL2 BINDING SITE, designated SEQ ID:13189, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66835] Another function of VGAM1958 is therefore inhibition of DRIL2 (Accession NM\_006465). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRIL2. EAT2 (Accession XM\_086490) is another VGAM1958 host target gene. EAT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EAT2 BINDING SITE, designated SEQ

ID:38708, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66836] Another function of VGAM1958 is therefore inhibition of EAT2 (Accession XM\_086490). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EAT2. EMILIN-2 (Accession NM\_032048) is another VGAM1958 host target gene. EMILIN-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EMILIN-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EMILIN-2 BINDING SITE, designated SEQ ID:25767, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66837] Another function of VGAM1958 is therefore inhibition of EMILIN-2 (Accession NM\_032048). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EMILIN-2. ENDOGLYX1 (Accession NM\_024756) is another VGAM1958 host target gene. ENDOGLYX1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENDOGLYX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENDOGLYX1 BINDING SITE, designated SEQ ID:24103, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66838] Another function of VGAM1958 is therefore inhibition of ENDOGLYX1 (Accession NM\_024756). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENDOGLYX1. Ets2 Repressor Factor (ERF, Accession NM\_006494) is another VGAM1958 host target gene. ERF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERF BINDING SITE, designated SEQ ID:13234, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66839] Another function of VGAM1958 is therefore inhibition of



Ets2 Repressor Factor (ERF, Accession NM\_006494). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERF. FEM-2 (Accession NM\_014634) is another VGAM1958 host target gene. FEM-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FEM-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FEM-2 BINDING SITE, designated SEQ ID:16006, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66840] Another function of VGAM1958 is therefore inhibition of FEM-2 (Accession NM\_014634). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FEM-2. Fidgetin-like 1 (FIGNL1, Accession NM\_022116) is another VGAM1958 host target gene. FIGNL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FIGNL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FIGNL1 BINDING SITE, designated SEQ ID:22661, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66841] Another function of VGAM1958 is therefore inhibition of Fidgetin-like 1 (FIGNL1, Accession NM\_022116). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FIGNL1. FKSG14 (Accession XM\_042025) is another VGAM1958 host target gene. FKSG14 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FKSG14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKSG14 BINDING SITE, designated SEQ ID:33670, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66842] Another function of VGAM1958 is therefore inhibition of FKSG14 (Accession XM\_042025). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKSG14. FLJ00024 (Accession XM\_033361) is another

VGAM1958 host target gene. FLJ00024 BINDING SITE1 and FLJ00024 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ00024, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00024 BINDING SITE1 and FLJ00024 BINDING SITE2, designated SEQ ID:31891 and SEQ ID:31894 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66843] Another function of VGAM1958 is therefore inhibition of FLJ00024 (Accession XM\_033361). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00024. FLJ10101 (Accession NM\_024718) is another VGAM1958 host target gene. FLJ10101 BINDING SITE1 and FLJ10101 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10101, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10101 BINDING SITE1 and FLJ10101

BINDING SITE2, designated SEQ ID:24044 and SEQ ID:24047 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66844] Another function of VGAM1958 is therefore inhibition of FLJ10101 (Accession NM\_024718). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10101. FLJ10342 (Accession NM\_018064) is another VGAM1958 host target gene. FLJ10342 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10342 BINDING SITE, designated SEQ ID:19834, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66845] Another function of VGAM1958 is therefore inhibition of FLJ10342 (Accession NM\_018064). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10342. FLJ10388 (Accession NM\_018082) is another

VGAM1958 host target gene. FLJ10388 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10388, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10388 BINDING SITE, designated SEQ ID:19842, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66846] Another function of VGAM1958 is therefore inhibition of FLJ10388 (Accession NM\_018082). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10388. FLJ10420 (Accession NM\_018090) is another VGAM1958 host target gene. FLJ10420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10420 BINDING SITE, designated SEQ ID:19858, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66847] Another function of VGAM1958 is therefore inhibition of FLJ10420 (Accession NM\_018090). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10420. FLJ10713 (Accession NM\_018189) is another VGAM1958 host target gene. FLJ10713 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10713 BINDING SITE, designated SEQ ID:20040, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66848] Another function of VGAM1958 is therefore inhibition of FLJ10713 (Accession NM\_018189). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10713. FLJ10751 (Accession NM\_018205) is another VGAM1958 host target gene. FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10751, corresponding to HOST TARGET binding sites

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2, designated SEQ ID:20095 and SEQ ID:20194 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66849] Another function of VGAM1958 is therefore inhibition of FLJ10751 (Accession NM\_018205). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10751. FLJ10803 (Accession NM\_018224) is another VGAM1958 host target gene. FLJ10803 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10803, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10803 BINDING SITE, designated SEQ ID:20152, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66850] Another function of VGAM1958 is therefore inhibition of FLJ10803 (Accession NM\_018224). Accordingly, utilities of

VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10803. FLJ10811 (Accession NM\_018228) is another VGAM1958 host target gene. FLJ10811 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10811 BINDING SITE, designated SEQ ID:20165, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66851] Another function of VGAM1958 is therefore inhibition of FLJ10811 (Accession NM\_018228). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10811. FLJ10829 (Accession NM\_018234) is another VGAM1958 host target gene. FLJ10829 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10829, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10829



BINDING SITE, designated SEQ ID:20180, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66852] Another function of VGAM1958 is therefore inhibition of FLJ10829 (Accession NM\_018234). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10829. FLJ10849 (Accession NM\_018243) is another VGAM1958 host target gene. FLJ10849 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10849, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10849 BINDING SITE, designated SEQ ID:20205, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66853] Another function of VGAM1958 is therefore inhibition of FLJ10849 (Accession NM\_018243). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10849. FLJ10895 (Accession NM\_019084) is another VGAM1958 host target gene. FLJ10895 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10895 BINDING SITE, designated SEQ ID:21158, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66854] Another function of VGAM1958 is therefore inhibition of FLJ10895 (Accession NM\_019084). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10895. FLJ10925 (Accession NM\_018275) is another VGAM1958 host target gene. FLJ10925 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10925 BINDING SITE, designated SEQ ID:20260, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66855] Another function of VGAM1958 is therefore inhibition of

FLJ10925 (Accession NM\_018275). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10925. FLJ11362 (Accession NM\_021946) is another VGAM1958 host target gene. FLJ11362 BINDING SITE1 and FLJ11362 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ11362, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11362 BINDING SITE1 and FLJ11362 BINDING SITE2, designated SEQ ID:22470 and SEQ ID:22472 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66856] Another function of VGAM1958 is therefore inhibition of FLJ11362 (Accession NM\_021946). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11362. FLJ11726 (Accession NM\_024971) is another VGAM1958 host target gene. FLJ11726 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11726, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11726 BINDING SITE, designated SEQ ID:24527, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66857] Another function of VGAM1958 is therefore inhibition of FLJ11726 (Accession NM\_024971). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11726. FLJ12057 (Accession NM\_024768) is another VGAM1958 host target gene. FLJ12057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12057 BINDING SITE, designated SEQ ID:24127, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66858] Another function of VGAM1958 is therefore inhibition of FLJ12057 (Accession NM\_024768). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ12057. FLJ12484 (Accession NM\_022767) is another VGAM1958 host target gene. FLJ12484 BINDING SITE1 through FLJ12484 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ12484, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12484 BINDING SITE1 through FLJ12484 BINDING SITE4, designated SEQ ID:23016, SEQ ID:23020, SEQ ID:34514 and SEQ ID:34518 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66859] Another function of VGAM1958 is therefore inhibition of FLJ12484 (Accession NM\_022767). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12484. FLJ12700 (Accession NM\_024910) is another VGAM1958 host target gene. FLJ12700 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ12700 BINDING SITE, designated SEQ ID:24413, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66860] Another function of VGAM1958 is therefore inhibition of FLJ12700 (Accession NM\_024910). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12700. FLJ12783 (Accession NM\_031426) is another VGAM1958 host target gene. FLJ12783 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12783, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12783 BINDING SITE, designated SEQ ID:25422, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66861] Another function of VGAM1958 is therefore inhibition of FLJ12783 (Accession NM\_031426). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12783. FLJ12960 (Accession NM\_024638) is another

VGAM1958 host target gene. FLJ12960 BINDING SITE1 and FLJ12960 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ12960, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12960 BINDING SITE1 and FLJ12960 BINDING SITE2, designated SEQ ID:23912 and SEQ ID:23916 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66862] Another function of VGAM1958 is therefore inhibition of FLJ12960 (Accession NM\_024638). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12960. FLJ13055 (Accession NM\_022737) is another VGAM1958 host target gene. FLJ13055 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13055, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13055 BINDING SITE, designated SEQ ID:22944, to the nucleotide

sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66863] Another function of VGAM1958 is therefore inhibition of FLJ13055 (Accession NM\_022737). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13055. FLJ13114 (Accession NM\_024541) is another VGAM1958 host target gene. FLJ13114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13114 BINDING SITE, designated SEQ ID:23750, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66864] Another function of VGAM1958 is therefore inhibition of FLJ13114 (Accession NM\_024541). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13114. FLJ13154 (Accession NM\_024598) is another VGAM1958 host target gene. FLJ13154 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by FLJ13154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13154 BINDING SITE, designated SEQ ID:23836, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66865] Another function of VGAM1958 is therefore inhibition of FLJ13154 (Accession NM\_024598). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13154. FLJ13189 (Accession NM\_024882) is another VGAM1958 host target gene. FLJ13189 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13189 BINDING SITE, designated SEQ ID:24327, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66866] Another function of VGAM1958 is therefore inhibition of FLJ13189 (Accession NM\_024882). Accordingly, utilities of

VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13189. FLJ13213 (Accession NM\_024755) is another VGAM1958 host target gene. FLJ13213 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13213 BINDING SITE, designated SEQ ID:24099, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66867] Another function of VGAM1958 is therefore inhibition of FLJ13213 (Accession NM\_024755). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13213. FLJ13224 (Accession NM\_024799) is another VGAM1958 host target gene. FLJ13224 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13224

BINDING SITE, designated SEQ ID:24177, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66868] Another function of VGAM1958 is therefore inhibition of FLJ13224 (Accession NM\_024799). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13224. FLJ13241 (Accession NM\_025088) is another VGAM1958 host target gene. FLJ13241 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13241 BINDING SITE, designated SEQ ID:24708, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66869] Another function of VGAM1958 is therefore inhibition of FLJ13241 (Accession NM\_025088). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13241. FLJ13262 (Accession NM\_024914) is another VGAM1958 host target gene. FLJ13262 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13262, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13262 BINDING SITE, designated SEQ ID:24432, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66870] Another function of VGAM1958 is therefore inhibition of FLJ13262 (Accession NM\_024914). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13262. FLJ13615 (Accession NM\_025114) is another VGAM1958 host target gene. FLJ13615 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ13615, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13615 BINDING SITE, designated SEQ ID:24763, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66871] Another function of VGAM1958 is therefore inhibition of

FLJ13615 (Accession NM\_025114). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13615. FLJ13659 (Accession NM\_025189) is another VGAM1958 host target gene. FLJ13659 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13659, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13659 BINDING SITE, designated SEQ ID:24832, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66872] Another function of VGAM1958 is therefore inhibition of FLJ13659 (Accession NM\_025189). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13659. FLJ13693 (Accession NM\_024807) is another VGAM1958 host target gene. FLJ13693 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ13693 BINDING SITE, designated SEQ ID:24185, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66873] Another function of VGAM1958 is therefore inhibition of FLJ13693 (Accession NM\_024807). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13693. FLJ13910 (Accession NM\_022780) is another VGAM1958 host target gene. FLJ13910 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13910 BINDING SITE, designated SEQ ID:23057, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66874] Another function of VGAM1958 is therefore inhibition of FLJ13910 (Accession NM\_022780). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13910. FLJ14106 (Accession NM\_025067) is another

VGAM1958 host target gene. FLJ14106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14106 BINDING SITE, designated SEQ ID:24665, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66875] Another function of VGAM1958 is therefore inhibition of FLJ14106 (Accession NM\_025067). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14106. FLJ14146 (Accession NM\_024709) is another VGAM1958 host target gene. FLJ14146 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14146 BINDING SITE, designated SEQ ID:24033, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66876] Another function of VGAM1958 is therefore inhibition of FLJ14146 (Accession NM\_024709). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14146. FLJ14327 (Accession NM\_024912) is another VGAM1958 host target gene. FLJ14327 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14327, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14327 BINDING SITE, designated SEQ ID:24420, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66877] Another function of VGAM1958 is therefore inhibition of FLJ14327 (Accession NM\_024912). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14327. FLJ14451 (Accession NM\_032786) is another VGAM1958 host target gene. FLJ14451 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14451 BINDING SITE, designated SEQ ID:26539, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66878] Another function of VGAM1958 is therefore inhibition of FLJ14451 (Accession NM\_032786). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14451. FLJ14564 (Accession XM\_084459) is another VGAM1958 host target gene. FLJ14564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14564 BINDING SITE, designated SEQ ID:37598, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66879] Another function of VGAM1958 is therefore inhibition of FLJ14564 (Accession XM\_084459). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ14564. FLJ14810 (Accession NM\_032843) is another VGAM1958 host target gene. FLJ14810 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14810, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14810 BINDING SITE, designated SEQ ID:26630, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66880] Another function of VGAM1958 is therefore inhibition of FLJ14810 (Accession NM\_032843). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14810. FLJ20034 (Accession NM\_017630) is another VGAM1958 host target gene. FLJ20034 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20034 BINDING SITE, designated SEQ ID:19129, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM

RNA, also designated SEQ ID:4669.

[66881] Another function of VGAM1958 is therefore inhibition of FLJ20034 (Accession NM\_017630). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20034. FLJ20040 (Accession NM\_018992) is another VGAM1958 host target gene. FLJ20040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20040 BINDING SITE, designated SEQ ID:21068, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66882] Another function of VGAM1958 is therefore inhibition of FLJ20040 (Accession NM\_018992). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20040. FLJ20294 (Accession NM\_017749) is another VGAM1958 host target gene. FLJ20294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20294, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20294 BINDING SITE, designated SEQ ID:19349, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66883] Another function of VGAM1958 is therefore inhibition of FLJ20294 (Accession NM\_017749). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20294. FLJ20298 (Accession NM\_017752) is another VGAM1958 host target gene. FLJ20298 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20298, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20298 BINDING SITE, designated SEQ ID:19364, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66884] Another function of VGAM1958 is therefore inhibition of FLJ20298 (Accession NM\_017752). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20298. FLJ20320 (Accession NM\_017765) is another VGAM1958 host target gene. FLJ20320 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20320 BINDING SITE, designated SEQ ID:19381, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66885] Another function of VGAM1958 is therefore inhibition of FLJ20320 (Accession NM\_017765). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20320. FLJ20375 (Accession NM\_017794) is another VGAM1958 host target gene. FLJ20375 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20375, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20375 BINDING SITE, designated SEQ ID:19432, to the nucleotide

sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66886] Another function of VGAM1958 is therefore inhibition of FLJ20375 (Accession NM\_017794). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20375. FLJ20401 (Accession NM\_017805) is another VGAM1958 host target gene. FLJ20401 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20401 BINDING SITE, designated SEQ ID:19447, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66887] Another function of VGAM1958 is therefore inhibition of FLJ20401 (Accession NM\_017805). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20401. FLJ20413 (Accession NM\_017808) is another VGAM1958 host target gene. FLJ20413 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ20413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20413 BINDING SITE, designated SEQ ID:19452, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66888] Another function of VGAM1958 is therefore inhibition of FLJ20413 (Accession NM\_017808). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20413. FLJ20421 (Accession NM\_017813) is another VGAM1958 host target gene. FLJ20421 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20421, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20421 BINDING SITE, designated SEQ ID:19461, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66889] Another function of VGAM1958 is therefore inhibition of FLJ20421 (Accession NM\_017813). Accordingly, utilities of

VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20421. FLJ20435 (Accession NM\_017821) is another VGAM1958 host target gene. FLJ20435 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20435 BINDING SITE, designated SEQ ID:19470, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66890] Another function of VGAM1958 is therefore inhibition of FLJ20435 (Accession NM\_017821). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20435. FLJ20508 (Accession NM\_017850) is another VGAM1958 host target gene. FLJ20508 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20508



BINDING SITE, designated SEQ ID:19519, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66891] Another function of VGAM1958 is therefore inhibition of FLJ20508 (Accession NM\_017850). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20508. FLJ20539 (Accession NM\_017870) is another VGAM1958 host target gene. FLJ20539 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20539, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20539 BINDING SITE, designated SEQ ID:19542, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66892] Another function of VGAM1958 is therefore inhibition of FLJ20539 (Accession NM\_017870). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20539. FLJ20584 (Accession NM\_017891) is another VGAM1958 host target gene. FLJ20584 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20584, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20584 BINDING SITE, designated SEQ ID:19557, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66893] Another function of VGAM1958 is therefore inhibition of FLJ20584 (Accession NM\_017891). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20584. FLJ20668 (Accession NM\_017923) is another VGAM1958 host target gene. FLJ20668 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20668 BINDING SITE, designated SEQ ID:19588, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66894] Another function of VGAM1958 is therefore inhibition of

FLJ20668 (Accession NM\_017923). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20668. FLJ20671 (Accession NM\_017924) is another VGAM1958 host target gene. FLJ20671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20671 BINDING SITE, designated SEQ ID:19591, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66895] Another function of VGAM1958 is therefore inhibition of FLJ20671 (Accession NM\_017924). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20671. FLJ20695 (Accession NM\_017929) is another VGAM1958 host target gene. FLJ20695 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20695, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ20695 BINDING SITE, designated SEQ ID:19614, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66896] Another function of VGAM1958 is therefore inhibition of FLJ20695 (Accession NM\_017929). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20695. FLJ20783 (Accession NM\_017958) is another VGAM1958 host target gene. FLJ20783 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20783, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20783 BINDING SITE, designated SEQ ID:19671, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66897] Another function of VGAM1958 is therefore inhibition of FLJ20783 (Accession NM\_017958). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20783. FLJ21032 (Accession NM\_024906) is another

VGAM1958 host target gene. FLJ21032 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21032 BINDING SITE, designated SEQ ID:24399, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66898] Another function of VGAM1958 is therefore inhibition of FLJ21032 (Accession NM\_024906). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21032. FLJ21324 (Accession XM\_165988) is another VGAM1958 host target gene. FLJ21324 BINDING SITE1 and FLJ21324 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ21324, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21324 BINDING SITE1 and FLJ21324 BINDING SITE2, designated SEQ ID:43827 and SEQ ID:43829 respectively, to the nucleotide sequence of

VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66899] Another function of VGAM1958 is therefore inhibition of FLJ21324 (Accession XM\_165988). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21324. FLJ21841 (Accession NM\_024609) is another VGAM1958 host target gene. FLJ21841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21841 BINDING SITE, designated SEQ ID:23863, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66900] Another function of VGAM1958 is therefore inhibition of FLJ21841 (Accession NM\_024609). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21841. FLJ22167 (Accession NM\_024533) is another VGAM1958 host target gene. FLJ22167 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ22167, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22167 BINDING SITE, designated SEQ ID:23741, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66901] Another function of VGAM1958 is therefore inhibition of FLJ22167 (Accession NM\_024533). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22167. FLJ22283 (Accession NM\_032220) is another VGAM1958 host target gene. FLJ22283 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22283 BINDING SITE, designated SEQ ID:25945, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66902] Another function of VGAM1958 is therefore inhibition of FLJ22283 (Accession NM\_032220). Accordingly, utilities of

VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22283. FLJ22405 (Accession NM\_022485) is another VGAM1958 host target gene. FLJ22405 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22405, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22405 BINDING SITE, designated SEQ ID:22865, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66903] Another function of VGAM1958 is therefore inhibition of FLJ22405 (Accession NM\_022485). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22405. FLJ22593 (Accession NM\_024703) is another VGAM1958 host target gene. FLJ22593 BINDING SITE1 and FLJ22593 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ22593, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide



sequences of FLJ22593 BINDING SITE1 and FLJ22593 BINDING SITE2, designated SEQ ID:24018 and SEQ ID:24019 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66904] Another function of VGAM1958 is therefore inhibition of FLJ22593 (Accession NM\_024703). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22593. FLJ22969 (Accession XM\_044006) is another VGAM1958 host target gene. FLJ22969 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22969, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22969 BINDING SITE, designated SEQ ID:34065, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66905] Another function of VGAM1958 is therefore inhibition of FLJ22969 (Accession XM\_044006). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ22969. FLJ23027 (Accession NM\_032233) is another VGAM1958 host target gene. FLJ23027 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23027, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23027 BINDING SITE, designated SEQ ID:25954, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66906] Another function of VGAM1958 is therefore inhibition of FLJ23027 (Accession NM\_032233). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23027. FLJ23058 (Accession NM\_024696) is another VGAM1958 host target gene. FLJ23058 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23058, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23058 BINDING SITE, designated SEQ ID:24004, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM

RNA, also designated SEQ ID:4669.

[66907] Another function of VGAM1958 is therefore inhibition of FLJ23058 (Accession NM\_024696). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23058. FLJ23129 (Accession NM\_024763) is another VGAM1958 host target gene. FLJ23129 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23129 BINDING SITE, designated SEQ ID:24121, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66908] Another function of VGAM1958 is therefore inhibition of FLJ23129 (Accession NM\_024763). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23129. FLJ23309 (Accession NM\_024896) is another VGAM1958 host target gene. FLJ23309 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23309, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23309 BINDING SITE, designated SEQ ID:24377, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66909] Another function of VGAM1958 is therefore inhibition of FLJ23309 (Accession NM\_024896). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23309. FLJ25416 (Accession NM\_145018) is another VGAM1958 host target gene. FLJ25416 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ25416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ25416 BINDING SITE, designated SEQ ID:29626, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66910] Another function of VGAM1958 is therefore inhibition of FLJ25416 (Accession NM\_145018). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ25416. FLJ31101 (Accession NM\_017964) is another VGAM1958 host target gene. FLJ31101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31101 BINDING SITE, designated SEQ ID:19683, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66911] Another function of VGAM1958 is therefore inhibition of FLJ31101 (Accession NM\_017964). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31101. FLJ32334 (Accession NM\_144565) is another VGAM1958 host target gene. FLJ32334 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32334, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32334 BINDING SITE, designated SEQ ID:29364, to the nucleotide

sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66912] Another function of VGAM1958 is therefore inhibition of FLJ32334 (Accession NM\_144565). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32334. Frequentin Homolog (Drosophila) (FREQ, Accession NM\_014286) is another VGAM1958 host target gene. FREQ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FREQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FREQ BINDING SITE, designated SEQ ID:15561, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66913] Another function of VGAM1958 is therefore inhibition of Frequentin Homolog (Drosophila) (FREQ, Accession NM\_014286). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FREQ. Far Upstream Element (FUSE) Binding Protein 3 (FUBP3, Accession XM\_033327) is another VGAM1958 host target gene.

FUBP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUBP3 BINDING SITE, designated SEQ ID:31877, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66914] Another function of VGAM1958 is therefore inhibition of Far Upstream Element (FUSE) Binding Protein 3 (FUBP3, Accession XM\_033327). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUBP3. GAPCENA (Accession NM\_012197) is another VGAM1958 host target gene. GAPCENA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAPCENA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAPCENA BINDING SITE, designated SEQ ID:14495, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4669.

[66915] Another function of VGAM1958 is therefore inhibition of GAPCENA (Accession NM\_012197). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAPCENA. GBTS1 (Accession NM\_145173) is another VGAM1958 host target gene. GBTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GBTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GBTS1 BINDING SITE, designated SEQ ID:29730, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66916] Another function of VGAM1958 is therefore inhibition of GBTS1 (Accession NM\_145173). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GBTS1. G Protein-coupled Receptor Kinase-interactor 1 (GIT1, Accession NM\_014030) is another VGAM1958 host target gene. GIT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by



GIT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT1 BINDING SITE, designated SEQ ID:15255, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66917] Another function of VGAM1958 is therefore inhibition of G Protein-coupled Receptor Kinase-interactor 1 (GIT1, Accession NM\_014030). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT1. Guanine Nucleotide Binding Protein (G protein), Gamma 4 (GNG4, Accession NM\_004485) is another VGAM1958 host target gene. GNG4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GNG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNG4 BINDING SITE, designated SEQ ID:10809, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66918] Another function of VGAM1958 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Gamma 4

(GNG4, Accession NM\_004485). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNG4. Glycoprotein V (platelet) (GP5, Accession NM\_004488) is another VGAM1958 host target gene. GP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GP5 BINDING SITE, designated SEQ ID:10823, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66919] Another function of VGAM1958 is therefore inhibition of Glycoprotein V (platelet) (GP5, Accession NM\_004488). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GP5. Glycoprotein A33 (transmembrane) (GPA33, Accession NM\_005814) is another VGAM1958 host target gene. GPA33 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPA33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPA33 BINDING SITE, designated SEQ ID:12405, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66920] Another function of VGAM1958 is therefore inhibition of Glycoprotein A33 (transmembrane) (GPA33, Accession NM\_005814). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPA33. GR6 (Accession NM\_007354) is another VGAM1958 host target gene. GR6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GR6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GR6 BINDING SITE, designated SEQ ID:14286, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66921] Another function of VGAM1958 is therefore inhibition of GR6 (Accession NM\_007354). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GR6.

GS3955 (Accession NM\_021643) is another VGAM1958 host target gene. GS3955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GS3955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GS3955 BINDING SITE, designated SEQ ID:22304, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66922] Another function of VGAM1958 is therefore inhibition of GS3955 (Accession NM\_021643). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GS3955. General Transcription Factor IIIC, Polypeptide 2, Beta 110kDa (GTF3C2, Accession NM\_001521) is another VGAM1958 host target gene. GTF3C2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GTF3C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTF3C2 BINDING SITE, designated SEQ ID:7262, to the nucleotide

sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66923] Another function of VGAM1958 is therefore inhibition of General Transcription Factor IIIC, Polypeptide 2, Beta 110kDa (GTF3C2, Accession NM\_001521). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTF3C2. H-L(3)MBT (Accession NM\_015478) is another VGAM1958 host target gene. H-L(3)MBT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H-L(3)MBT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H-L(3)MBT BINDING SITE, designated SEQ ID:17754, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66924] Another function of VGAM1958 is therefore inhibition of H-L(3)MBT (Accession NM\_015478). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H-L(3)MBT. H-plk (Accession NM\_015852) is another VGAM1958 host target gene. H-plk BINDING SITE is HOST

TARGET binding site found in the 5` untranslated region of mRNA encoded by H-plk, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H-plk BINDING SITE, designated SEQ ID:17982, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66925] Another function of VGAM1958 is therefore inhibition of H-plk (Accession NM\_015852). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H-plk. HCA4 (Accession XM\_085287) is another VGAM1958 host target gene. HCA4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA4 BINDING SITE, designated SEQ ID:38028, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66926] Another function of VGAM1958 is therefore inhibition of

HCA4 (Accession XM\_085287). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCA4. Hect Domain and RLD 3 (HERC3, Accession NM\_014606) is another VGAM1958 host target gene. HERC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HERC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HERC3 BINDING SITE, designated SEQ ID:15971, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66927] Another function of VGAM1958 is therefore inhibition of Hect Domain and RLD 3 (HERC3, Accession NM\_014606). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HERC3. Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM\_014571) is another VGAM1958 host target gene. HEYL BINDING SITE1 and HEYL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HEYL, corresponding to HOST TARGET binding sites such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEYL BINDING SITE1 and HEYL BINDING SITE2, designated SEQ ID:15927 and SEQ ID:15933 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66928] Another function of VGAM1958 is therefore inhibition of Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM\_014571). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEYL. HRIHFB2436 (Accession NM\_014345) is another VGAM1958 host target gene. HRIHFB2436 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HRIHFB2436, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRIHFB2436 BINDING SITE, designated SEQ ID:15664, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66929] Another function of VGAM1958 is therefore inhibition of HRIHFB2436 (Accession NM\_014345). Accordingly, utili-



ties of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRIHFB2436. HSA404617 (Accession XM\_052600) is another VGAM1958 host target gene. HSA404617 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSA404617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA404617 BINDING SITE, designated SEQ ID:36002, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66930] Another function of VGAM1958 is therefore inhibition of HSA404617 (Accession XM\_052600). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA404617. HSNOV1 (Accession NM\_017515) is another VGAM1958 host target gene. HSNOV1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSNOV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSNOV1

BINDING SITE, designated SEQ ID:18966, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66931] Another function of VGAM1958 is therefore inhibition of HSNOV1 (Accession NM\_017515). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSNOV1. Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM\_014424) is another VGAM1958 host target gene. HSPB7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPB7 BINDING SITE, designated SEQ ID:15781, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66932] Another function of VGAM1958 is therefore inhibition of Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM\_014424). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with HSPB7. HSPC055 (Accession NM\_014153) is another VGAM1958 host target gene. HSPC055 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPC055, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC055 BINDING SITE, designated SEQ ID:15435, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66933] Another function of VGAM1958 is therefore inhibition of HSPC055 (Accession NM\_014153). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC055. HSU79303 (Accession NM\_013301) is another VGAM1958 host target gene. HSU79303 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSU79303, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSU79303 BINDING SITE, designated SEQ ID:14961, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[66934] Another function of VGAM1958 is therefore inhibition of HSU79303 (Accession NM\_013301). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSU79303. Integrin, Beta 8 (ITGB8, Accession NM\_002214) is another VGAM1958 host target gene. ITGB8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ITGB8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGB8 BINDING SITE, designated SEQ ID:7979, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66935] Another function of VGAM1958 is therefore inhibition of Integrin, Beta 8 (ITGB8, Accession NM\_002214). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGB8. Junctional Adhesion Molecule 1 (JAM1, Accession NM\_016946) is another VGAM1958 host target gene. JAM1 BINDING SITE1 through JAM1 BINDING SITE4 are HOST TARGET binding sites found in untranslated re-

gions of mRNA encoded by JAM1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAM1 BINDING SITE1 through JAM1 BINDING SITE4, designated SEQ ID:18858, SEQ ID:29325, SEQ ID:29334 and SEQ ID:29345 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66936] Another function of VGAM1958 is therefore inhibition of Junctional Adhesion Molecule 1 (JAM1, Accession NM\_016946). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAM1. Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 1 (KCNS1, Accession NM\_002251) is another VGAM1958 host target gene. KCNS1 BINDING SITE1 and KCNS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KCNS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNS1 BINDING SITE1 and KCNS1 BINDING SITE2, desig-

nated SEQ ID:8044 and SEQ ID:8047 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66937] Another function of VGAM1958 is therefore inhibition of Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 1 (KCNS1, Accession NM\_002251). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNS1. KH Domain Containing, RNA Binding, Signal Transduction Associated 3 (KHDRBS3, Accession NM\_006558) is another VGAM1958 host target gene. KHDRBS3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KHDRBS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KHDRBS3 BINDING SITE, designated SEQ ID:13326, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66938] Another function of VGAM1958 is therefore inhibition of KH Domain Containing, RNA Binding, Signal Transduction Associated 3 (KHDRBS3, Accession NM\_006558). Accord-

ingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KHDRBS3. KIAA0014 (Accession NM\_014665) is another VGAM1958 host target gene. KIAA0014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0014 BINDING SITE, designated SEQ ID:16115, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66939] Another function of VGAM1958 is therefore inhibition of KIAA0014 (Accession NM\_014665). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0014. KIAA0053 (Accession NM\_014882) is another VGAM1958 host target gene. KIAA0053 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0053, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0053 BINDING SITE, designated SEQ ID:17031, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66940] Another function of VGAM1958 is therefore inhibition of KIAA0053 (Accession NM\_014882). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0053. KIAA0121 (Accession XM\_052386) is another VGAM1958 host target gene. KIAA0121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0121 BINDING SITE, designated SEQ ID:35970, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66941] Another function of VGAM1958 is therefore inhibition of KIAA0121 (Accession XM\_052386). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0121. KIAA0141 (Accession NM\_014773) is another VGAM1958 host target gene. KIAA0141 BINDING SITE1



and KIAA0141 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0141, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0141 BINDING SITE1 and KIAA0141 BINDING SITE2, designated SEQ ID:16583 and SEQ ID:16585 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66942] Another function of VGAM1958 is therefore inhibition of KIAA0141 (Accession NM\_014773). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0141. KIAA0146 (Accession XM\_088282) is another VGAM1958 host target gene. KIAA0146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0146 BINDING SITE, designated SEQ ID:39583, to the nucleotide sequence of VGAM1958 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4669.

[66943] Another function of VGAM1958 is therefore inhibition of KIAA0146 (Accession XM\_088282). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0146. KIAA0152 (Accession NM\_014730) is another VGAM1958 host target gene. KIAA0152 BINDING SITE1 and KIAA0152 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0152, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0152 BINDING SITE1 and KIAA0152 BINDING SITE2, designated SEQ ID:16334 and SEQ ID:16339 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66944] Another function of VGAM1958 is therefore inhibition of KIAA0152 (Accession NM\_014730). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0152. KIAA0161 (Accession NM\_014746) is another VGAM1958 host target gene. KIAA0161 BINDING SITE1

and KIAA0161 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0161, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0161 BINDING SITE1 and KIAA0161 BINDING SITE2, designated SEQ ID:16431 and SEQ ID:32824 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66945] Another function of VGAM1958 is therefore inhibition of KIAA0161 (Accession NM\_014746). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0161. KIAA0247 (Accession NM\_014734) is another VGAM1958 host target gene. KIAA0247 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0247 BINDING SITE, designated SEQ ID:16375, to the nucleotide sequence of VGAM1958 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4669.

[66946] Another function of VGAM1958 is therefore inhibition of KIAA0247 (Accession NM\_014734). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0247. KIAA0265 (Accession XM\_045954) is another VGAM1958 host target gene. KIAA0265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0265 BINDING SITE, designated SEQ ID:34623, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66947] Another function of VGAM1958 is therefore inhibition of KIAA0265 (Accession XM\_045954). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0265. KIAA0266 (Accession NM\_021645) is another VGAM1958 host target gene. KIAA0266 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0266, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0266 BINDING SITE, designated SEQ ID:22308, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66948] Another function of VGAM1958 is therefore inhibition of KIAA0266 (Accession NM\_021645). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0266. KIAA0298 (Accession XM\_084529) is another VGAM1958 host target gene. KIAA0298 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0298, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0298 BINDING SITE, designated SEQ ID:37626, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66949] Another function of VGAM1958 is therefore inhibition of KIAA0298 (Accession XM\_084529). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0298. KIAA0318 (Accession XM\_044334) is another VGAM1958 host target gene. KIAA0318 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0318 BINDING SITE, designated SEQ ID:34186, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66950] Another function of VGAM1958 is therefore inhibition of KIAA0318 (Accession XM\_044334). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0318. KIAA0321 (Accession XM\_031077) is another VGAM1958 host target gene. KIAA0321 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0321, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0321 BINDING SITE, designated SEQ ID:31266, to the

nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66951] Another function of VGAM1958 is therefore inhibition of KIAA0321 (Accession XM\_031077). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0321. KIAA0335 (Accession NM\_014803) is another VGAM1958 host target gene. KIAA0335 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0335 BINDING SITE, designated SEQ ID:16733, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66952] Another function of VGAM1958 is therefore inhibition of KIAA0335 (Accession NM\_014803). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0335. KIAA0349 (Accession XM\_166449) is another VGAM1958 host target gene. KIAA0349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0349 BINDING SITE, designated SEQ ID:44341, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66953] Another function of VGAM1958 is therefore inhibition of KIAA0349 (Accession XM\_166449). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0349. KIAA0390 (Accession NM\_014717) is another VGAM1958 host target gene. KIAA0390 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0390, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0390 BINDING SITE, designated SEQ ID:16270, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66954] Another function of VGAM1958 is therefore inhibition of KIAA0390 (Accession NM\_014717). Accordingly, utilities



of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0390. KIAA0420 (Accession XM\_032693) is another VGAM1958 host target gene. KIAA0420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0420 BINDING SITE, designated SEQ ID:31722, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66955] Another function of VGAM1958 is therefore inhibition of KIAA0420 (Accession XM\_032693). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0420. KIAA0430 (Accession NM\_019081) is another VGAM1958 host target gene. KIAA0430 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0430 BINDING SITE, designated SEQ ID:21151, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66956] Another function of VGAM1958 is therefore inhibition of KIAA0430 (Accession NM\_019081). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0430. KIAA0444 (Accession XM\_030999) is another VGAM1958 host target gene. KIAA0444 BINDING SITE1 through KIAA0444 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0444, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0444 BINDING SITE1 through KIAA0444 BINDING SITE4, designated SEQ ID:31239, SEQ ID:31241, SEQ ID:31243 and SEQ ID:31245 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66957] Another function of VGAM1958 is therefore inhibition of KIAA0444 (Accession XM\_030999). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0444. KIAA0493 (Accession XM\_034717) is another VGAM1958 host target gene. KIAA0493 BINDING SITE1 and KIAA0493 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0493, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0493 BINDING SITE1 and KIAA0493 BINDING SITE2, designated SEQ ID:32136 and SEQ ID:32137 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66958] Another function of VGAM1958 is therefore inhibition of KIAA0493 (Accession XM\_034717). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0493. KIAA0515 (Accession XM\_033380) is another VGAM1958 host target gene. KIAA0515 BINDING SITE1 and KIAA0515 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0515, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of KIAA0515 BINDING SITE1 and KIAA0515 BINDING SITE2, designated SEQ ID:31916 and SEQ ID:31919 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66959] Another function of VGAM1958 is therefore inhibition of KIAA0515 (Accession XM\_033380). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0515. KIAA0552 (Accession NM\_014731) is another VGAM1958 host target gene. KIAA0552 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0552, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0552 BINDING SITE, designated SEQ ID:16349, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66960] Another function of VGAM1958 is therefore inhibition of KIAA0552 (Accession NM\_014731). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0552. KIAA0557 (Accession XM\_085507) is another VGAM1958 host target gene. KIAA0557 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0557 BINDING SITE, designated SEQ ID:38205, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66961] Another function of VGAM1958 is therefore inhibition of KIAA0557 (Accession XM\_085507). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0557. KIAA0560 (Accession XM\_029045) is another VGAM1958 host target gene. KIAA0560 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0560, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0560 BINDING SITE, designated SEQ ID:30837, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[66962] Another function of VGAM1958 is therefore inhibition of KIAA0560 (Accession XM\_029045). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0560. KIAA0562 (Accession NM\_014704) is another VGAM1958 host target gene. KIAA0562 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0562, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0562 BINDING SITE, designated SEQ ID:16240, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66963] Another function of VGAM1958 is therefore inhibition of KIAA0562 (Accession NM\_014704). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0562. KIAA0596 (Accession XM\_031706) is another VGAM1958 host target gene. KIAA0596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0596, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0596 BINDING SITE, designated SEQ ID:31463, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66964] Another function of VGAM1958 is therefore inhibition of KIAA0596 (Accession XM\_031706). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0596. KIAA0632 (Accession NM\_015545) is another VGAM1958 host target gene. KIAA0632 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0632, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0632 BINDING SITE, designated SEQ ID:17808, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66965] Another function of VGAM1958 is therefore inhibition of KIAA0632 (Accession NM\_015545). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0632. KIAA0638 (Accession XM\_051489) is another VGAM1958 host target gene. KIAA0638 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0638, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0638 BINDING SITE, designated SEQ ID:35845, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66966] Another function of VGAM1958 is therefore inhibition of KIAA0638 (Accession XM\_051489). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0638. KIAA0668 (Accession XM\_039332) is another VGAM1958 host target gene. KIAA0668 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0668 BINDING SITE, designated SEQ ID:33051, to the



nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66967] Another function of VGAM1958 is therefore inhibition of KIAA0668 (Accession XM\_039332). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0668. KIAA0676 (Accession NM\_015043) is another VGAM1958 host target gene. KIAA0676 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0676, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0676 BINDING SITE, designated SEQ ID:17394, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66968] Another function of VGAM1958 is therefore inhibition of KIAA0676 (Accession NM\_015043). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0676. KIAA0682 (Accession NM\_014852) is another VGAM1958 host target gene. KIAA0682 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0682 BINDING SITE, designated SEQ ID:16899, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66969] Another function of VGAM1958 is therefore inhibition of KIAA0682 (Accession NM\_014852). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0682. KIAA0720 (Accession XM\_030970) is another VGAM1958 host target gene. KIAA0720 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0720 BINDING SITE, designated SEQ ID:31234, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66970] Another function of VGAM1958 is therefore inhibition of KIAA0720 (Accession XM\_030970). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0720. KIAA0729 (Accession XM\_171027) is another VGAM1958 host target gene. KIAA0729 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0729, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0729 BINDING SITE, designated SEQ ID:45805, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66971] Another function of VGAM1958 is therefore inhibition of KIAA0729 (Accession XM\_171027). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0729. KIAA0759 (Accession XM\_041090) is another VGAM1958 host target gene. KIAA0759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0759 BINDING SITE, designated SEQ ID:33440, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66972] Another function of VGAM1958 is therefore inhibition of KIAA0759 (Accession XM\_041090). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0759. KIAA0767 (Accession XM\_027105) is another VGAM1958 host target gene. KIAA0767 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0767, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0767 BINDING SITE, designated SEQ ID:30408, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66973] Another function of VGAM1958 is therefore inhibition of KIAA0767 (Accession XM\_027105). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0767. KIAA0773 (Accession NM\_014690) is another VGAM1958 host target gene. KIAA0773 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0773 BINDING SITE, designated SEQ ID:16192, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66974] Another function of VGAM1958 is therefore inhibition of KIAA0773 (Accession NM\_014690). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0773. KIAA0806 (Accession NM\_014813) is another VGAM1958 host target gene. KIAA0806 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0806, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0806 BINDING SITE, designated SEQ ID:16780, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66975] Another function of VGAM1958 is therefore inhibition of

KIAA0806 (Accession NM\_014813). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0806. KIAA0819 (Accession XM\_032996) is another VGAM1958 host target gene. KIAA0819 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0819, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0819 BINDING SITE, designated SEQ ID:31809, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66976] Another function of VGAM1958 is therefore inhibition of KIAA0819 (Accession XM\_032996). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0819. KIAA0831 (Accession NM\_014924) is another VGAM1958 host target gene. KIAA0831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0831 BINDING SITE, designated SEQ ID:17208, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66977] Another function of VGAM1958 is therefore inhibition of KIAA0831 (Accession NM\_014924). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0831. KIAA0870 (Accession XM\_088315) is another VGAM1958 host target gene. KIAA0870 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0870 BINDING SITE, designated SEQ ID:39608, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66978] Another function of VGAM1958 is therefore inhibition of KIAA0870 (Accession XM\_088315). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0870. KIAA0923 (Accession NM\_014021) is another

VGAM1958 host target gene. KIAA0923 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0923 BINDING SITE, designated SEQ ID:15245, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66979] Another function of VGAM1958 is therefore inhibition of KIAA0923 (Accession NM\_014021). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0923. KIAA0924 (Accession NM\_014897) is another VGAM1958 host target gene. KIAA0924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0924 BINDING SITE, designated SEQ ID:17065, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.



[66980] Another function of VGAM1958 is therefore inhibition of KIAA0924 (Accession NM\_014897). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0924. KIAA0953 (Accession XM\_039733) is another VGAM1958 host target gene. KIAA0953 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0953, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0953 BINDING SITE, designated SEQ ID:33165, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66981] Another function of VGAM1958 is therefore inhibition of KIAA0953 (Accession XM\_039733). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0953. KIAA0978 (Accession XM\_047013) is another VGAM1958 host target gene. KIAA0978 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0978, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0978 BINDING SITE, designated SEQ ID:34891, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66982] Another function of VGAM1958 is therefore inhibition of KIAA0978 (Accession XM\_047013). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0978. KIAA1014 (Accession XM\_037205) is another VGAM1958 host target gene. KIAA1014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1014 BINDING SITE, designated SEQ ID:32569, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66983] Another function of VGAM1958 is therefore inhibition of KIAA1014 (Accession XM\_037205). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1014. KIAA1036 (Accession NM\_014909) is another VGAM1958 host target gene. KIAA1036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1036 BINDING SITE, designated SEQ ID:17129, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66984] Another function of VGAM1958 is therefore inhibition of KIAA1036 (Accession NM\_014909). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1036. KIAA1041 (Accession NM\_014947) is another VGAM1958 host target gene. KIAA1041 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1041, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1041 BINDING SITE, designated SEQ ID:17267, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[66985] Another function of VGAM1958 is therefore inhibition of KIAA1041 (Accession NM\_014947). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1041. KIAA1045 (Accession XM\_048592) is another VGAM1958 host target gene. KIAA1045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1045 BINDING SITE, designated SEQ ID:35192, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66986] Another function of VGAM1958 is therefore inhibition of KIAA1045 (Accession XM\_048592). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1045. KIAA1052 (Accession NM\_014956) is another VGAM1958 host target gene. KIAA1052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1052, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1052 BINDING SITE, designated SEQ ID:17313, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66987] Another function of VGAM1958 is therefore inhibition of KIAA1052 (Accession NM\_014956). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1052. KIAA1077 (Accession XM\_053496) is another VGAM1958 host target gene. KIAA1077 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1077 BINDING SITE, designated SEQ ID:36098, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66988] Another function of VGAM1958 is therefore inhibition of KIAA1077 (Accession XM\_053496). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1077. KIAA1118 (Accession XM\_045581) is another VGAM1958 host target gene. KIAA1118 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1118, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1118 BINDING SITE, designated SEQ ID:34486, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66989] Another function of VGAM1958 is therefore inhibition of KIAA1118 (Accession XM\_045581). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1118. KIAA1128 (Accession XM\_043596) is another VGAM1958 host target gene. KIAA1128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1128 BINDING SITE, designated SEQ ID:33973, to the

nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66990] Another function of VGAM1958 is therefore inhibition of KIAA1128 (Accession XM\_043596). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1128. KIAA1130 (Accession XM\_031104) is another VGAM1958 host target gene. KIAA1130 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1130 BINDING SITE, designated SEQ ID:31284, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66991] Another function of VGAM1958 is therefore inhibition of KIAA1130 (Accession XM\_031104). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1130. KIAA1143 (Accession XM\_044014) is another VGAM1958 host target gene. KIAA1143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1143 BINDING SITE, designated SEQ ID:34075, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66992] Another function of VGAM1958 is therefore inhibition of KIAA1143 (Accession XM\_044014). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1143. KIAA1161 (Accession XM\_088501) is another VGAM1958 host target gene. KIAA1161 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1161 BINDING SITE, designated SEQ ID:39746, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66993] Another function of VGAM1958 is therefore inhibition of KIAA1161 (Accession XM\_088501). Accordingly, utilities



of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1161. KIAA1181 (Accession XM\_043340) is another VGAM1958 host target gene. KIAA1181 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1181 BINDING SITE, designated SEQ ID:33923, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66994] Another function of VGAM1958 is therefore inhibition of KIAA1181 (Accession XM\_043340). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1181. KIAA1185 (Accession XM\_031399) is another VGAM1958 host target gene. KIAA1185 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1185, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1185 BINDING SITE, designated SEQ ID:31370, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66995] Another function of VGAM1958 is therefore inhibition of KIAA1185 (Accession XM\_031399). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1185. KIAA1196 (Accession XM\_028968) is another VGAM1958 host target gene. KIAA1196 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1196 BINDING SITE, designated SEQ ID:30818, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66996] Another function of VGAM1958 is therefore inhibition of KIAA1196 (Accession XM\_028968). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1196. KIAA1211 (Accession XM\_044178) is another VGAM1958 host target gene. KIAA1211 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1211 BINDING SITE, designated SEQ ID:34165, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66997] Another function of VGAM1958 is therefore inhibition of KIAA1211 (Accession XM\_044178). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1211. KIAA1228 (Accession XM\_036408) is another VGAM1958 host target gene. KIAA1228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1228 BINDING SITE, designated SEQ ID:32439, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66998] Another function of VGAM1958 is therefore inhibition of

KIAA1228 (Accession XM\_036408). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1228. KIAA1277 (Accession XM\_035114) is another VGAM1958 host target gene. KIAA1277 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1277 BINDING SITE, designated SEQ ID:32204, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[66999] Another function of VGAM1958 is therefore inhibition of KIAA1277 (Accession XM\_035114). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1277. KIAA1280 (Accession XM\_045766) is another VGAM1958 host target gene. KIAA1280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1280 BINDING SITE, designated SEQ ID:34558, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67000] Another function of VGAM1958 is therefore inhibition of KIAA1280 (Accession XM\_045766). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1280. KIAA1322 (Accession XM\_052626) is another VGAM1958 host target gene. KIAA1322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1322 BINDING SITE, designated SEQ ID:36032, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67001] Another function of VGAM1958 is therefore inhibition of KIAA1322 (Accession XM\_052626). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1322. KIAA1332 (Accession XM\_048774) is another

VGAM1958 host target gene. KIAA1332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1332 BINDING SITE, designated SEQ ID:35257, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67002] Another function of VGAM1958 is therefore inhibition of KIAA1332 (Accession XM\_048774). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1332. KIAA1348 (Accession XM\_043826) is another VGAM1958 host target gene. KIAA1348 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1348, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1348 BINDING SITE, designated SEQ ID:34029, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67003] Another function of VGAM1958 is therefore inhibition of KIAA1348 (Accession XM\_043826). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1348. KIAA1432 (Accession XM\_039698) is another VGAM1958 host target gene. KIAA1432 BINDING SITE1 and KIAA1432 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1432, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1432 BINDING SITE1 and KIAA1432 BINDING SITE2, designated SEQ ID:33145 and SEQ ID:33148 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67004] Another function of VGAM1958 is therefore inhibition of KIAA1432 (Accession XM\_039698). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1432. KIAA1493 (Accession XM\_034415) is another VGAM1958 host target gene. KIAA1493 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1493 BINDING SITE, designated SEQ ID:32086, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67005] Another function of VGAM1958 is therefore inhibition of KIAA1493 (Accession XM\_034415). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1493. KIAA1560 (Accession XM\_034422) is another VGAM1958 host target gene. KIAA1560 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1560, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1560 BINDING SITE, designated SEQ ID:32099, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67006] Another function of VGAM1958 is therefore inhibition of KIAA1560 (Accession XM\_034422). Accordingly, utilities



of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1560. KIAA1571 (Accession XM\_027744) is another VGAM1958 host target gene. KIAA1571 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1571, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1571 BINDING SITE, designated SEQ ID:30563, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67007] Another function of VGAM1958 is therefore inhibition of KIAA1571 (Accession XM\_027744). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1571. KIAA1576 (Accession XM\_038186) is another VGAM1958 host target gene. KIAA1576 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1576 BINDING SITE, designated SEQ ID:32771, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67008] Another function of VGAM1958 is therefore inhibition of KIAA1576 (Accession XM\_038186). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1576. KIAA1610 (Accession XM\_040622) is another VGAM1958 host target gene. KIAA1610 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1610, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1610 BINDING SITE, designated SEQ ID:33337, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67009] Another function of VGAM1958 is therefore inhibition of KIAA1610 (Accession XM\_040622). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1610. KIAA1656 (Accession XM\_038022) is another VGAM1958 host target gene. KIAA1656 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1656 BINDING SITE, designated SEQ ID:32733, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67010] Another function of VGAM1958 is therefore inhibition of KIAA1656 (Accession XM\_038022). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1656. KIAA1719 (Accession XM\_042936) is another VGAM1958 host target gene. KIAA1719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33820, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67011] Another function of VGAM1958 is therefore inhibition of

KIAA1719 (Accession XM\_042936). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. KIAA1750 (Accession XM\_043067) is another VGAM1958 host target gene. KIAA1750 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1750 BINDING SITE, designated SEQ ID:33877, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67012] Another function of VGAM1958 is therefore inhibition of KIAA1750 (Accession XM\_043067). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1750. KIAA1754 (Accession XM\_032587) is another VGAM1958 host target gene. KIAA1754 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1754, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1754 BINDING SITE, designated SEQ ID:31680, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67013] Another function of VGAM1958 is therefore inhibition of KIAA1754 (Accession XM\_032587). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1754. KIAA1814 (Accession XM\_046822) is another VGAM1958 host target gene. KIAA1814 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1814, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1814 BINDING SITE, designated SEQ ID:34837, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67014] Another function of VGAM1958 is therefore inhibition of KIAA1814 (Accession XM\_046822). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1814. KIAA1821 (Accession XM\_050101) is another

VGAM1958 host target gene. KIAA1821 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1821, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1821 BINDING SITE, designated SEQ ID:35550, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67015] Another function of VGAM1958 is therefore inhibition of KIAA1821 (Accession XM\_050101). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1821. KIAA1854 (Accession XM\_049884) is another VGAM1958 host target gene. KIAA1854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35530, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67016] Another function of VGAM1958 is therefore inhibition of KIAA1854 (Accession XM\_049884). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. KIAA1887 (Accession XM\_084801) is another VGAM1958 host target gene. KIAA1887 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1887, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1887 BINDING SITE, designated SEQ ID:37713, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67017] Another function of VGAM1958 is therefore inhibition of KIAA1887 (Accession XM\_084801). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1887. KIAA1894 (Accession XM\_058025) is another VGAM1958 host target gene. KIAA1894 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1894, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1894 BINDING SITE, designated SEQ ID:36559, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67018] Another function of VGAM1958 is therefore inhibition of KIAA1894 (Accession XM\_058025). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1894. KIAA1904 (Accession XM\_056282) is another VGAM1958 host target gene. KIAA1904 BINDING SITE1 and KIAA1904 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1904, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1904 BINDING SITE1 and KIAA1904 BINDING SITE2, designated SEQ ID:36378 and SEQ ID:36379 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67019] Another function of VGAM1958 is therefore inhibition of KIAA1904 (Accession XM\_056282). Accordingly, utilities



of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1904. KIAA1924 (Accession XM\_057091) is another VGAM1958 host target gene. KIAA1924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1924 BINDING SITE, designated SEQ ID:36474, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67020] Another function of VGAM1958 is therefore inhibition of KIAA1924 (Accession XM\_057091). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1924. KIAA1940 (Accession XM\_086981) is another VGAM1958 host target gene. KIAA1940 BINDING SITE1 and KIAA1940 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1940, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of KIAA1940 BINDING SITE1 and KIAA1940 BINDING SITE2, designated SEQ ID:39003 and SEQ ID:39007 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67021] Another function of VGAM1958 is therefore inhibition of KIAA1940 (Accession XM\_086981). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1940. KOC1 (Accession XM\_165847) is another VGAM1958 host target gene. KOC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KOC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KOC1 BINDING SITE, designated SEQ ID:43780, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67022] Another function of VGAM1958 is therefore inhibition of KOC1 (Accession XM\_165847). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KOC1.

Keratin Associated Protein 1–5 (KRTAP1–5, Accession NM\_031957) is another VGAM1958 host target gene. KRTAP1–5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KRTAP1–5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KRTAP1–5 BINDING SITE, designated SEQ ID:25697, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67023] Another function of VGAM1958 is therefore inhibition of Keratin Associated Protein 1–5 (KRTAP1–5, Accession NM\_031957). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KRTAP1–5. I(3)mbt-like (Drosophila) (L3MBTL, Accession XM\_045421) is another VGAM1958 host target gene. L3MBTL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by L3MBTL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of L3MBTL

BINDING SITE, designated SEQ ID:34456, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67024] Another function of VGAM1958 is therefore inhibition of I(3)mbt-like (Drosophila) (L3MBTL, Accession XM\_045421). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with L3MBTL. I(3)mbt-like 2 (Drosophila) (L3MBTL2, Accession XM\_114201) is another VGAM1958 host target gene. L3MBTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by L3MBTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of L3MBTL2 BINDING SITE, designated SEQ ID:42790, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67025] Another function of VGAM1958 is therefore inhibition of I(3)mbt-like 2 (Drosophila) (L3MBTL2, Accession XM\_114201). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with L3MBTL2. Lysosomal-asso-

ciated Membrane Protein 3 (LAMP3, Accession XM\_003022) is another VGAM1958 host target gene. LAMP3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LAMP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMP3 BINDING SITE, designated SEQ ID:29919, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67026] Another function of VGAM1958 is therefore inhibition of Lysosomal-associated Membrane Protein 3 (LAMP3, Accession XM\_003022). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAMP3. LIM and SH3 Protein 1 (LASP1, Accession NM\_006148) is another VGAM1958 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LASP1 BINDING SITE,

designated SEQ ID:12797, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67027] Another function of VGAM1958 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM\_006148). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. Leucine-rich Repeat LGI Family, Member 3 (LGI3, Accession NM\_139278) is another VGAM1958 host target gene. LGI3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LGI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGI3 BINDING SITE, designated SEQ ID:29278, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67028] Another function of VGAM1958 is therefore inhibition of Leucine-rich Repeat LGI Family, Member 3 (LGI3, Accession NM\_139278). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGI3. Mitogen-activated

Protein Kinase Kinase 3 (MAP2K3, Accession NM\_145109) is another VGAM1958 host target gene. MAP2K3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MAP2K3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K3 BINDING SITE, designated SEQ ID:29715, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67029] Another function of VGAM1958 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 3 (MAP2K3, Accession NM\_145109). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K3. Mitogen-activated Protein Kinase Kinase Kinase 3 (MAP3K3, Accession NM\_002401) is another VGAM1958 host target gene. MAP3K3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAP3K3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K3 BINDING SITE, designated SEQ

ID:8222, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67030] Another function of VGAM1958 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 3 (MAP3K3, Accession NM\_002401). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K3. MAWBP (Accession NM\_022129) is another VGAM1958 host target gene. MAWBP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAWBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAWBP BINDING SITE, designated SEQ ID:22680, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67031] Another function of VGAM1958 is therefore inhibition of MAWBP (Accession NM\_022129). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAWBP. MBLL39 (Accession NM\_144778) is another



VGAM1958 host target gene. MBLL39 BINDING SITE1 through MBLL39 BINDING SITE7 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MBLL39, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBLL39 BINDING SITE1 through MBLL39 BINDING SITE7, designated SEQ ID:29568, SEQ ID:29571, SEQ ID:29572, SEQ ID:29578, SEQ ID:12317, SEQ ID:12318 and SEQ ID:12321 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67032] Another function of VGAM1958 is therefore inhibition of MBLL39 (Accession NM\_144778). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBLL39. MGC:5244 (Accession NM\_031213) is another VGAM1958 host target gene. MGC:5244 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC:5244, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC:5244 BINDING SITE, designated SEQ ID:25258, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67033] Another function of VGAM1958 is therefore inhibition of MGC:5244 (Accession NM\_031213). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC:5244. MGC10765 (Accession NM\_024345) is another VGAM1958 host target gene. MGC10765 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10765, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10765 BINDING SITE, designated SEQ ID:23646, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67034] Another function of VGAM1958 is therefore inhibition of MGC10765 (Accession NM\_024345). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10765. MGC11034 (Accession NM\_031453) is another VGAM1958 host target gene. MGC11034 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC11034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11034 BINDING SITE, designated SEQ ID:25470, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67035] Another function of VGAM1958 is therefore inhibition of MGC11034 (Accession NM\_031453). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11034. MGC12335 (Accession NM\_032744) is another VGAM1958 host target gene. MGC12335 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC12335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12335 BINDING SITE, designated SEQ ID:26477, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67036] Another function of VGAM1958 is therefore inhibition of

MGC12335 (Accession NM\_032744). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12335. MGC12679 (Accession NM\_032733) is another VGAM1958 host target gene. MGC12679 BINDING SITE1 and MGC12679 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MGC12679, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12679 BINDING SITE1 and MGC12679 BINDING SITE2, designated SEQ ID:26457 and SEQ ID:26459 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67037] Another function of VGAM1958 is therefore inhibition of MGC12679 (Accession NM\_032733). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12679. MGC13090 (Accession NM\_032711) is another VGAM1958 host target gene. MGC13090 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13090, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13090 BINDING SITE, designated SEQ ID:26427, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67038] Another function of VGAM1958 is therefore inhibition of MGC13090 (Accession NM\_032711). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13090. MGC13170 (Accession NM\_032712) is another VGAM1958 host target gene. MGC13170 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC13170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13170 BINDING SITE, designated SEQ ID:26432, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67039] Another function of VGAM1958 is therefore inhibition of MGC13170 (Accession NM\_032712). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC13170. MGC14161 (Accession NM\_032892) is another VGAM1958 host target gene. MGC14161 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC14161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14161 BINDING SITE, designated SEQ ID:26716, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67040] Another function of VGAM1958 is therefore inhibition of MGC14161 (Accession NM\_032892). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14161. MGC14407 (Accession NM\_032908) is another VGAM1958 host target gene. MGC14407 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC14407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14407 BINDING SITE, designated SEQ ID:26729, to

the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67041] Another function of VGAM1958 is therefore inhibition of MGC14407 (Accession NM\_032908). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14407. MGC15476 (Accession NM\_145056) is another VGAM1958 host target gene. MGC15476 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15476 BINDING SITE, designated SEQ ID:29691, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67042] Another function of VGAM1958 is therefore inhibition of MGC15476 (Accession NM\_145056). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15476. MGC16169 (Accession NM\_033115) is another VGAM1958 host target gene. MGC16169 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by MGC16169, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16169 BINDING SITE, designated SEQ ID:26963, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67043] Another function of VGAM1958 is therefore inhibition of MGC16169 (Accession NM\_033115). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16169. MGC16491 (Accession NM\_052943) is another VGAM1958 host target gene. MGC16491 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC16491, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16491 BINDING SITE, designated SEQ ID:27501, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67044] Another function of VGAM1958 is therefore inhibition of MGC16491 (Accession NM\_052943). Accordingly, utilities



of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16491. MGC1842 (Accession XM\_037797) is another VGAM1958 host target gene. MGC1842 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC1842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC1842 BINDING SITE, designated SEQ ID:32685, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67045] Another function of VGAM1958 is therefore inhibition of MGC1842 (Accession XM\_037797). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC1842. MGC20253 (Accession NM\_144583) is another VGAM1958 host target gene. MGC20253 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20253, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC20253 BINDING SITE, designated SEQ ID:29399, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67046] Another function of VGAM1958 is therefore inhibition of MGC20253 (Accession NM\_144583). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20253. MGC20470 (Accession NM\_145053) is another VGAM1958 host target gene. MGC20470 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20470, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20470 BINDING SITE, designated SEQ ID:29687, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67047] Another function of VGAM1958 is therefore inhibition of MGC20470 (Accession NM\_145053). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20470. MGC21854 (Accession NM\_052862) is another VGAM1958 host target gene. MGC21854 BINDING

SITE is HOST TARGET binding site found in the 3` un-translated region of mRNA encoded by MGC21854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC21854 BINDING SITE, designated SEQ ID:27447, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67048] Another function of VGAM1958 is therefore inhibition of MGC21854 (Accession NM\_052862). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC21854. MGC21945 (Accession NM\_145057) is another VGAM1958 host target gene. MGC21945 BINDING SITE is HOST TARGET binding site found in the 5` un-translated region of mRNA encoded by MGC21945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC21945 BINDING SITE, designated SEQ ID:29692, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67049] Another function of VGAM1958 is therefore inhibition of

MGC21945 (Accession NM\_145057). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC21945. MGC22014 (Accession XM\_035307) is another VGAM1958 host target gene. MGC22014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC22014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC22014 BINDING SITE, designated SEQ ID:32220, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67050] Another function of VGAM1958 is therefore inhibition of MGC22014 (Accession XM\_035307). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC22014. MGC2306 (Accession NM\_032638) is another VGAM1958 host target gene. MGC2306 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC2306 BINDING SITE, designated SEQ ID:26354, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67051] Another function of VGAM1958 is therefore inhibition of MGC2306 (Accession NM\_032638). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2306. MGC2452 (Accession NM\_032644) is another VGAM1958 host target gene. MGC2452 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2452 BINDING SITE, designated SEQ ID:26363, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67052] Another function of VGAM1958 is therefore inhibition of MGC2452 (Accession NM\_032644). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2452. MGC3113 (Accession NM\_024035) is another

VGAM1958 host target gene. MGC3113 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC3113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3113 BINDING SITE, designated SEQ ID:23468, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67053] Another function of VGAM1958 is therefore inhibition of MGC3113 (Accession NM\_024035). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3113. MGC33182 (Accession XM\_062903) is another VGAM1958 host target gene. MGC33182 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC33182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC33182 BINDING SITE, designated SEQ ID:37235, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67054] Another function of VGAM1958 is therefore inhibition of MGC33182 (Accession XM\_062903). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC33182. MGC35558 (Accession NM\_145013) is another VGAM1958 host target gene. MGC35558 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC35558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC35558 BINDING SITE, designated SEQ ID:29613, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67055] Another function of VGAM1958 is therefore inhibition of MGC35558 (Accession NM\_145013). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC35558. MGC4342 (Accession NM\_024329) is another VGAM1958 host target gene. MGC4342 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC4342, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4342 BINDING SITE, designated SEQ ID:23626, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67056] Another function of VGAM1958 is therefore inhibition of MGC4342 (Accession NM\_024329). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4342. MGC4504 (Accession NM\_024111) is another VGAM1958 host target gene. MGC4504 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4504 BINDING SITE, designated SEQ ID:23561, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67057] Another function of VGAM1958 is therefore inhibition of MGC4504 (Accession NM\_024111). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with



MGC4504. MGC4549 (Accession NM\_032377) is another VGAM1958 host target gene. MGC4549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4549 BINDING SITE, designated SEQ ID:26170, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67058] Another function of VGAM1958 is therefore inhibition of MGC4549 (Accession NM\_032377). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4549. MGC4604 (Accession NM\_031487) is another VGAM1958 host target gene. MGC4604 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4604, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4604 BINDING SITE, designated SEQ ID:25577, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM

RNA, also designated SEQ ID:4669.

[67059] Another function of VGAM1958 is therefore inhibition of MGC4604 (Accession NM\_031487). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4604. MGC4643 (Accession NM\_032715) is another VGAM1958 host target gene. MGC4643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4643 BINDING SITE, designated SEQ ID:26444, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67060] Another function of VGAM1958 is therefore inhibition of MGC4643 (Accession NM\_032715). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4643. MGC4796 (Accession XM\_029031) is another VGAM1958 host target gene. MGC4796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4796, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4796 BINDING SITE, designated SEQ ID:30833, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67061] Another function of VGAM1958 is therefore inhibition of MGC4796 (Accession XM\_029031). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4796. MGC5601 (Accession NM\_025247) is another VGAM1958 host target gene. MGC5601 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC5601, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5601 BINDING SITE, designated SEQ ID:24926, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67062] Another function of VGAM1958 is therefore inhibition of MGC5601 (Accession NM\_025247). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC5601. MIC2 Like 1 (MIC2L1, Accession NM\_031462) is another VGAM1958 host target gene. MIC2L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MIC2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIC2L1 BINDING SITE, designated SEQ ID:25488, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67063] Another function of VGAM1958 is therefore inhibition of MIC2 Like 1 (MIC2L1, Accession NM\_031462). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIC2L1. MIG-6 (Accession NM\_018948) is another VGAM1958 host target gene. MIG-6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MIG-6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIG-6 BINDING SITE, designated SEQ ID:21020, to the nucleotide se-

quence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67064] Another function of VGAM1958 is therefore inhibition of MIG-6 (Accession NM\_018948). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIG-6. MOST2 (Accession NM\_020250) is another VGAM1958 host target gene. MOST2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MOST2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOST2 BINDING SITE, designated SEQ ID:21549, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67065] Another function of VGAM1958 is therefore inhibition of MOST2 (Accession NM\_020250). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOST2. MST4 (Accession NM\_016542) is another VGAM1958 host target gene. MST4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by MST4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MST4 BINDING SITE, designated SEQ ID:18609, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67066] Another function of VGAM1958 is therefore inhibition of MST4 (Accession NM\_016542). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MST4. MY014 (Accession NM\_030918) is another VGAM1958 host target gene. MY014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MY014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MY014 BINDING SITE, designated SEQ ID:25188, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67067] Another function of VGAM1958 is therefore inhibition of MY014 (Accession NM\_030918). Accordingly, utilities of

VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MY014. N4BP3 (Accession XM\_038920) is another VGAM1958 host target gene. N4BP3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by N4BP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP3 BINDING SITE, designated SEQ ID:32934, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67068] Another function of VGAM1958 is therefore inhibition of N4BP3 (Accession XM\_038920). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP3. Neuroblastoma, Suppression of Tumorigenicity 1 (NBL1, Accession XM\_001434) is another VGAM1958 host target gene. NBL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NBL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of NBL1 BINDING SITE, designated SEQ ID:29838, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67069] Another function of VGAM1958 is therefore inhibition of Neuroblastoma, Suppression of Tumorigenicity 1 (NBL1, Accession XM\_001434). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBL1. NCKX3 (Accession NM\_020689) is another VGAM1958 host target gene. NCKX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCKX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCKX3 BINDING SITE, designated SEQ ID:21840, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67070] Another function of VGAM1958 is therefore inhibition of NCKX3 (Accession NM\_020689). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCKX3. NECL1 (Accession NM\_021189) is another VGAM1958 host



target gene. NECL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NECL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NECL1 BINDING SITE, designated SEQ ID:22165, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67071] Another function of VGAM1958 is therefore inhibition of NECL1 (Accession NM\_021189). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NECL1. NIBAN (Accession NM\_022083) is another VGAM1958 host target gene. NIBAN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NIBAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIBAN BINDING SITE, designated SEQ ID:22627, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67072] Another function of VGAM1958 is therefore inhibition of NIBAN (Accession NM\_022083). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIBAN. NIN283 (Accession NM\_032268) is another VGAM1958 host target gene. NIN283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NIN283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIN283 BINDING SITE, designated SEQ ID:26012, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67073] Another function of VGAM1958 is therefore inhibition of NIN283 (Accession NM\_032268). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIN283. Ninjurin 2 (NINJ2, Accession NM\_016533) is another VGAM1958 host target gene. NINJ2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NINJ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NINJ2 BINDING SITE, designated SEQ ID:18604, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67074] Another function of VGAM1958 is therefore inhibition of Ninjurin 2 (NINJ2, Accession NM\_016533). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NINJ2. NIP30 (Accession NM\_024946) is another VGAM1958 host target gene. NIP30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NIP30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIP30 BINDING SITE, designated SEQ ID:24499, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67075] Another function of VGAM1958 is therefore inhibition of NIP30 (Accession NM\_024946). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIP30.

NKIR (Accession NM\_139018) is another VGAM1958 host target gene. NKIR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NKIR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NKIR BINDING SITE, designated SEQ ID:29117, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67076] Another function of VGAM1958 is therefore inhibition of NKIR (Accession NM\_139018). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NKIR. NPD009 (Accession XM\_170795) is another VGAM1958 host target gene. NPD009 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NPD009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPD009 BINDING SITE, designated SEQ ID:45560, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4669.

[67077] Another function of VGAM1958 is therefore inhibition of NPD009 (Accession XM\_170795). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPD009. Neuronal Pentraxin Receptor (NPTXR, Accession NM\_014293) is another VGAM1958 host target gene. NPTXR BINDING SITE1 and NPTXR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NPTXR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPTXR BINDING SITE1 and NPTXR BINDING SITE2, designated SEQ ID:15583 and SEQ ID:27731 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67078] Another function of VGAM1958 is therefore inhibition of Neuronal Pentraxin Receptor (NPTXR, Accession NM\_014293). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPTXR. Nucleoredoxin (NXN, Accession NM\_022463) is another VGAM1958 host

target gene. NXN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXN BINDING SITE, designated SEQ ID:22810, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67079] Another function of VGAM1958 is therefore inhibition of Nucleoredoxin (NXN, Accession NM\_022463). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXN. Neurexophilin 3 (NXPH3, Accession XM\_037847) is another VGAM1958 host target gene. NXPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXPH3 BINDING SITE, designated SEQ ID:32713, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ

ID:4669.

[67080] Another function of VGAM1958 is therefore inhibition of Neurexophilin 3 (NXPH3, Accession XM\_037847). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXPH3. NY-REN-25 (Accession XM\_027116) is another VGAM1958 host target gene. NY-REN-25 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NY-REN-25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-25 BINDING SITE, designated SEQ ID:30421, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67081] Another function of VGAM1958 is therefore inhibition of NY-REN-25 (Accession XM\_027116). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-25. OCIA (Accession NM\_017830) is another VGAM1958 host target gene. OCIA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OCIA, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OCIA BINDING SITE, designated SEQ ID:19492, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67082] Another function of VGAM1958 is therefore inhibition of OCIA (Accession NM\_017830). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OCIA. Opiate Receptor-like 1 (OPRL1, Accession NM\_000913) is another VGAM1958 host target gene. OPRL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPRL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPRL1 BINDING SITE, designated SEQ ID:6617, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67083] Another function of VGAM1958 is therefore inhibition of Opiate Receptor-like 1 (OPRL1, Accession NM\_000913). Accordingly, utilities of VGAM1958 include diagnosis,



prevention and treatment of diseases and clinical conditions associated with OPRL1. Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM\_040635) is another VGAM1958 host target gene. P2RX1 BINDING SITE1 and P2RX1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by P2RX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RX1 BINDING SITE1 and P2RX1 BINDING SITE2, designated SEQ ID:33356 and SEQ ID:33357 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67084] Another function of VGAM1958 is therefore inhibition of Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM\_040635). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RX1. Period Homolog 3 (Drosophila) (PER3, Accession NM\_016831) is another VGAM1958 host target gene. PER3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PER3, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER3 BINDING SITE, designated SEQ ID:18824, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67085] Another function of VGAM1958 is therefore inhibition of Period Homolog 3 (Drosophila) (PER3, Accession NM\_016831). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER3. Protease Inhibitor 15 (PI15, Accession NM\_015886) is another VGAM1958 host target gene. PI15 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PI15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PI15 BINDING SITE, designated SEQ ID:18029, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67086] Another function of VGAM1958 is therefore inhibition of Protease Inhibitor 15 (PI15, Accession NM\_015886). Ac-

cordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PI15. PILR(ALPHA) (Accession NM\_013439) is another VGAM1958 host target gene. PILR(ALPHA) BINDING SITE1 and PILR(ALPHA) BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PILR(ALPHA), corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PILR(ALPHA) BINDING SITE1 and PILR(ALPHA) BINDING SITE2, designated SEQ ID:15101 and SEQ ID:15102 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67087] Another function of VGAM1958 is therefore inhibition of PILR(ALPHA) (Accession NM\_013439). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PILR(ALPHA). PIP3-E (Accession XM\_039749) is another VGAM1958 host target gene. PIP3-E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP3-E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP3-E BINDING SITE, designated SEQ ID:33177, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67088] Another function of VGAM1958 is therefore inhibition of PIP3-E (Accession XM\_039749). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP3-E. Phosphatidylserine Decarboxylase (PISD, Accession NM\_014338) is another VGAM1958 host target gene. PISD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PISD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PISD BINDING SITE, designated SEQ ID:15653, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67089] Another function of VGAM1958 is therefore inhibition of Phosphatidylserine Decarboxylase (PISD, Accession NM\_014338). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with PISD. PM5 (Accession XM\_027359) is another VGAM1958 host target gene. PM5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PM5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PM5 BINDING SITE, designated SEQ ID:30496, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67090] Another function of VGAM1958 is therefore inhibition of PM5 (Accession XM\_027359). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PM5. Paraneoplastic Antigen Like 5 (PNMA5, Accession XM\_057016) is another VGAM1958 host target gene. PNMA5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PNMA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PNMA5 BINDING SITE, designated SEQ ID:36442, to the nucleotide sequence of VGAM1958 RNA,

herein designated VGAM RNA, also designated SEQ ID:4669.

[67091] Another function of VGAM1958 is therefore inhibition of Paraneoplastic Antigen Like 5 (PNMA5, Accession XM\_057016). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PNMA5. POLA2 (Accession NM\_002689) is another VGAM1958 host target gene. POLA2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by POLA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLA2 BINDING SITE, designated SEQ ID:8548, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67092] Another function of VGAM1958 is therefore inhibition of POLA2 (Accession NM\_002689). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLA2. PP2447 (Accession NM\_025204) is another VGAM1958 host target gene. PP2447 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by PP2447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP2447 BINDING SITE, designated SEQ ID:24869, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67093] Another function of VGAM1958 is therefore inhibition of PP2447 (Accession NM\_025204). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP2447. Protein Phosphatase 1A (formerly 2C), Magnesium-dependent, Alpha Isoform (PPM1A, Accession NM\_021003) is another VGAM1958 host target gene. PPM1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPM1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPM1A BINDING SITE, designated SEQ ID:21998, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67094] Another function of VGAM1958 is therefore inhibition of Protein Phosphatase 1A (formerly 2C), Magnesium-dependent, Alpha Isoform (PPM1A, Accession NM\_021003). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPM1A. Protein Phosphatase 1, Regulatory Subunit 10 (PPP1R10, Accession NM\_002714) is another VGAM1958 host target gene. PPP1R10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R10 BINDING SITE, designated SEQ ID:8573, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67095] Another function of VGAM1958 is therefore inhibition of Protein Phosphatase 1, Regulatory Subunit 10 (PPP1R10, Accession NM\_002714). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R10. Protein Phosphatase 4, Regulatory Subunit 1-like (PPP4R1L, Accession XM\_086650) is another



VGAM1958 host target gene. PPP4R1L BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PPP4R1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP4R1L BINDING SITE, designated SEQ ID:38815, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67096] Another function of VGAM1958 is therefore inhibition of Protein Phosphatase 4, Regulatory Subunit 1-like (PPP4R1L, Accession XM\_086650). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP4R1L. PR Domain Containing 7 (PRDM7, Accession NM\_052996) is another VGAM1958 host target gene. PRDM7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRDM7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM7 BINDING SITE, designated SEQ ID:27568, to the nucleotide sequence of VGAM1958 RNA,

herein designated VGAM RNA, also designated SEQ ID:4669.

[67097] Another function of VGAM1958 is therefore inhibition of PR Domain Containing 7 (PRDM7, Accession NM\_052996). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM7. PRIC285 (Accession XM\_028918) is another VGAM1958 host target gene. PRIC285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRIC285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRIC285 BINDING SITE, designated SEQ ID:30805, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67098] Another function of VGAM1958 is therefore inhibition of PRIC285 (Accession XM\_028918). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRIC285. Protein Kinase, Lysine Deficient 2 (PRKWINK2, Accession XM\_117531) is another VGAM1958 host target

gene. PRKWNK2 BINDING SITE1 and PRKWNK2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PRKWNK2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKWNK2 BINDING SITE1 and PRKWNK2 BINDING SITE2, designated SEQ ID:43518 and SEQ ID:43522 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67099] Another function of VGAM1958 is therefore inhibition of Protein Kinase, Lysine Deficient 2 (PRKWNK2, Accession XM\_117531). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKWNK2. PRO1598 (Accession NM\_018503) is another VGAM1958 host target gene. PRO1598 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1598 BINDING SITE, designated SEQ ID:20568, to the nucleotide sequence of VGAM1958

RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67100] Another function of VGAM1958 is therefore inhibition of PRO1598 (Accession NM\_018503). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1598. PRO2214 (Accession NM\_018517) is another VGAM1958 host target gene. PRO2214 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO2214, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2214 BINDING SITE, designated SEQ ID:20587, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67101] Another function of VGAM1958 is therefore inhibition of PRO2214 (Accession NM\_018517). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2214. PRO2900 (Accession NM\_018635) is another VGAM1958 host target gene. PRO2900 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by PRO2900, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2900 BINDING SITE, designated SEQ ID:20707, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67102] Another function of VGAM1958 is therefore inhibition of PRO2900 (Accession NM\_018635). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2900. PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM\_028335) is another VGAM1958 host target gene. PRPF8 BINDING SITE1 and PRPF8 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PRPF8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPF8 BINDING SITE1 and PRPF8 BINDING SITE2, designated SEQ ID:30674 and SEQ ID:30682 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ

ID:4669.

[67103] Another function of VGAM1958 is therefore inhibition of PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM\_028335). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRPF8. PSR (Accession XM\_036784) is another VGAM1958 host target gene. PSR BINDING SITE1 and PSR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PSR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSR BINDING SITE1 and PSR BINDING SITE2, designated SEQ ID:32496 and SEQ ID:32499 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67104] Another function of VGAM1958 is therefore inhibition of PSR (Accession XM\_036784). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSR. PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession NM\_005975) is another VGAM1958 host target gene.

PTK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTK6 BINDING SITE, designated SEQ ID:12595, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67105] Another function of VGAM1958 is therefore inhibition of PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession NM\_005975). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTK6. RA-GEF-2 (Accession NM\_016340) is another VGAM1958 host target gene. RA-GEF-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RA-GEF-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RA-GEF-2 BINDING SITE, designated SEQ ID:18461, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67106] Another function of VGAM1958 is therefore inhibition of RA-GEF-2 (Accession NM\_016340). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RA-GEF-2. RAB34, Member RAS Oncogene Family (RAB34, Accession NM\_031934) is another VGAM1958 host target gene. RAB34 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB34 BINDING SITE, designated SEQ ID:25682, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67107] Another function of VGAM1958 is therefore inhibition of RAB34, Member RAS Oncogene Family (RAB34, Accession NM\_031934). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB34. RAB3D, Member RAS Oncogene Family (RAB3D, Accession NM\_004283) is another VGAM1958 host target gene. RAB3D BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by RAB3D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB3D BINDING SITE, designated SEQ ID:10496, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67108] Another function of VGAM1958 is therefore inhibition of RAB3D, Member RAS Oncogene Family (RAB3D, Accession NM\_004283). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB3D. RALGPS1A (Accession NM\_014636) is another VGAM1958 host target gene. RALGPS1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RALGPS1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RALGPS1A BINDING SITE, designated SEQ ID:16018, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67109] Another function of VGAM1958 is therefore inhibition of

RALGPS1A (Accession NM\_014636). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RALGPS1A. Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM\_014737) is another VGAM1958 host target gene. RASSF2 BINDING SITE1 and RASSF2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RASSF2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASSF2 BINDING SITE1 and RASSF2 BINDING SITE2, designated SEQ ID:16387 and SEQ ID:16395 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67110] Another function of VGAM1958 is therefore inhibition of Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM\_014737). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASSF2. RLUCL (Accession NM\_058192) is another VGAM1958 host target gene. RLUCL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by RLUC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RLUC BINDING SITE, designated SEQ ID:27755, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67111] Another function of VGAM1958 is therefore inhibition of RLUC (Accession NM\_058192). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RLUC. Roundabout Homolog 4, Magic Roundabout (Drosophila) (ROBO4, Accession NM\_019055) is another VGAM1958 host target gene. ROBO4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ROBO4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROBO4 BINDING SITE, designated SEQ ID:21135, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67112] Another function of VGAM1958 is therefore inhibition of

Roundabout Homolog 4, Magic Roundabout (Drosophila) (ROBO4, Accession NM\_019055). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROBO4. SAD1 (Accession XM\_034123) is another VGAM1958 host target gene. SAD1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SAD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SAD1 BINDING SITE, designated SEQ ID:32009, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67113] Another function of VGAM1958 is therefore inhibition of SAD1 (Accession XM\_034123). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAD1. SAST (Accession XM\_032034) is another VGAM1958 host target gene. SAST BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SAST, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SAST BINDING SITE, designated SEQ ID:31541, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67114] Another function of VGAM1958 is therefore inhibition of SAST (Accession XM\_032034). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAST. SCAMP-4 (Accession NM\_079834) is another VGAM1958 host target gene. SCAMP-4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCAMP-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAMP-4 BINDING SITE, designated SEQ ID:27821, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67115] Another function of VGAM1958 is therefore inhibition of SCAMP-4 (Accession NM\_079834). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

SCAMP-4. SCAMP5 (Accession NM\_138967) is another VGAM1958 host target gene. SCAMP5 BINDING SITE1 and SCAMP5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SCAMP5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAMP5 BINDING SITE1 and SCAMP5 BINDING SITE2, designated SEQ ID:29076 and SEQ ID:29077 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67116] Another function of VGAM1958 is therefore inhibition of SCAMP5 (Accession NM\_138967). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCAMP5. Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654) is another VGAM1958 host target gene. SDC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of SDC3 BINDING SITE, designated SEQ ID:16087, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67117] Another function of VGAM1958 is therefore inhibition of Syndecan 3 (N-syndecan) (SDC3, Accession NM\_014654). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC3. SEF (Accession XM\_045300) is another VGAM1958 host target gene. SEF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEF BINDING SITE, designated SEQ ID:34427, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67118] Another function of VGAM1958 is therefore inhibition of SEF (Accession XM\_045300). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEF. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain,

(semaphorin) 4B (SEMA4B, Accession XM\_044533) is another VGAM1958 host target gene. SEMA4B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4B BINDING SITE, designated SEQ ID:34226, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67119] Another function of VGAM1958 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4B (SEMA4B, Accession XM\_044533). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4B. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM\_004263) is another VGAM1958 host target gene. SEMA4F BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA4F, corresponding to a HOST TARGET binding site



such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4F BINDING SITE, designated SEQ ID:10457, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67120] Another function of VGAM1958 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM\_004263). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4F. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4G (SEMA4G, Accession XM\_170638) is another VGAM1958 host target gene. SEMA4G BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEMA4G, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4G BINDING SITE, designated SEQ ID:45412, to the nucleotide sequence of VGAM1958 RNA,

herein designated VGAM RNA, also designated SEQ ID:4669.

[67121] Another function of VGAM1958 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4G (SEMA4G, Accession XM\_170638). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4G. Sema Domain, Seven Thrombospondin Repeats (type 1 and type 1-like), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 5A (SEMA5A, Accession NM\_003966) is another VGAM1958 host target gene. SEMA5A BINDING SITE1 and SEMA5A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SEMA5A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA5A BINDING SITE1 and SEMA5A BINDING SITE2, designated SEQ ID:10104 and SEQ ID:10106 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67122] Another function of VGAM1958 is therefore inhibition of Sema Domain, Seven Thrombospondin Repeats (type 1 and type 1-like), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 5A (SEMA5A, Accession NM\_003966). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA5A. SEP15 (Accession NM\_004261) is another VGAM1958 host target gene. SEP15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEP15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEP15 BINDING SITE, designated SEQ ID:10452, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67123] Another function of VGAM1958 is therefore inhibition of SEP15 (Accession NM\_004261). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEP15. Small EDRK-rich Factor 1B (centromeric) (SERF1B, Accession NM\_022978) is another VGAM1958 host target gene.

SERF1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERF1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERF1B BINDING SITE, designated SEQ ID:23260, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67124] Another function of VGAM1958 is therefore inhibition of Small EDRK-rich Factor 1B (centromeric) (SERF1B, Accession NM\_022978). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERF1B. Splicing Factor, Arginine/serine-rich 12 (SFRS12, Accession NM\_139168) is another VGAM1958 host target gene. SFRS12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SFRS12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS12 BINDING SITE, designated SEQ ID:29177, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[67125] Another function of VGAM1958 is therefore inhibition of Splicing Factor, Arginine/serine-rich 12 (SFRS12, Accession NM\_139168). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS12. SH3 and Multiple Ankyrin Repeat Domains 3 (SHANK3, Accession XM\_037493) is another VGAM1958 host target gene. SHANK3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SHANK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHANK3 BINDING SITE, designated SEQ ID:32634, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67126] Another function of VGAM1958 is therefore inhibition of SH3 and Multiple Ankyrin Repeat Domains 3 (SHANK3, Accession XM\_037493). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHANK3. ShrmL (Accession NM\_020859) is another VGAM1958 host target

gene. ShrmL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ShrmL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ShrmL BINDING SITE, designated SEQ ID:21911, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67127] Another function of VGAM1958 is therefore inhibition of ShrmL (Accession NM\_020859). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ShrmL. Solute Carrier Family 12, (potassium–chloride transporter) Member 5 (SLC12A5, Accession NM\_020708) is another VGAM1958 host target gene. SLC12A5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC12A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC12A5 BINDING SITE, designated SEQ ID:21852, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM

RNA, also designated SEQ ID:4669.

[67128] Another function of VGAM1958 is therefore inhibition of Solute Carrier Family 12, (potassium–chloride transporter) Member 5 (SLC12A5, Accession NM\_020708). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A5. Solute Carrier Family 26, Member 10 (SLC26A10, Accession NM\_133489) is another VGAM1958 host target gene. SLC26A10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC26A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A10 BINDING SITE, designated SEQ ID:28562, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67129] Another function of VGAM1958 is therefore inhibition of Solute Carrier Family 26, Member 10 (SLC26A10, Accession NM\_133489). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A10. Solute Carrier Family 38, Member 5 (SLC38A5, Accession

NM\_033518) is another VGAM1958 host target gene. SLC38A5 BINDING SITE1 and SLC38A5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC38A5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC38A5 BINDING SITE1 and SLC38A5 BINDING SITE2, designated SEQ ID:27297 and SEQ ID:27299 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67130] Another function of VGAM1958 is therefore inhibition of Solute Carrier Family 38, Member 5 (SLC38A5, Accession NM\_033518). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC38A5. Synaptosomal-associated Protein, 29kDa (SNAP29, Accession NM\_004782) is another VGAM1958 host target gene. SNAP29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNAP29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of



SNAP29 BINDING SITE, designated SEQ ID:11188, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67131] Another function of VGAM1958 is therefore inhibition of Synaptosomal-associated Protein, 29kDa (SNAP29, Accession NM\_004782). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAP29. Synaptosomal-associated Protein, 91kDa Homolog (mouse) (SNAP91, Accession NM\_014841) is another VGAM1958 host target gene. SNAP91 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNAP91, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAP91 BINDING SITE, designated SEQ ID:16870, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67132] Another function of VGAM1958 is therefore inhibition of Synaptosomal-associated Protein, 91kDa Homolog (mouse) (SNAP91, Accession NM\_014841). Accordingly, utilities of VGAM1958 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with SNAP91. Syntaphilin (SNPH, Accession NM\_014723) is another VGAM1958 host target gene. SNPH BINDING SITE1 and SNPH BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SNPH, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNPH BINDING SITE1 and SNPH BINDING SITE2, designated SEQ ID:16287 and SEQ ID:16299 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67133] Another function of VGAM1958 is therefore inhibition of Syntaphilin (SNPH, Accession NM\_014723). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNPH. Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM\_004863) is another VGAM1958 host target gene. SPTLC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTLC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of SPTLC2 BINDING SITE, designated SEQ ID:11282, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67134] Another function of VGAM1958 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM\_004863). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. SSH2 (Accession XM\_030846) is another VGAM1958 host target gene. SSH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSH2 BINDING SITE, designated SEQ ID:31183, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67135] Another function of VGAM1958 is therefore inhibition of SSH2 (Accession XM\_030846). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH2.

Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 2 (STAM2, Accession NM\_005843) is another VGAM1958 host target gene. STAM2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAM2 BINDING SITE, designated SEQ ID:12459, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67136] Another function of VGAM1958 is therefore inhibition of Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 2 (STAM2, Accession NM\_005843). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAM2. START Domain Containing 7 (STARD7, Accession NM\_020151) is another VGAM1958 host target gene. STARD7 BINDING SITE1 and STARD7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by STARD7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of STARD7 BINDING SITE1 and STARD7 BINDING SITE2, designated SEQ ID:21359 and SEQ ID:29261 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67137] Another function of VGAM1958 is therefore inhibition of START Domain Containing 7 (STARD7, Accession NM\_020151). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STARD7. Stromal Interaction Molecule 2 (STIM2, Accession NM\_020860) is another VGAM1958 host target gene. STIM2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STIM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STIM2 BINDING SITE, designated SEQ ID:21914, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67138] Another function of VGAM1958 is therefore inhibition of Stromal Interaction Molecule 2 (STIM2, Accession NM\_020860). Accordingly, utilities of VGAM1958 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with STIM2. Stomatin (EPB72)-like 1 (STOML1, Accession NM\_004809) is another VGAM1958 host target gene. STOML1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STOML1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STOML1 BINDING SITE, designated SEQ ID:11232, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67139] Another function of VGAM1958 is therefore inhibition of Stomatin (EPB72)-like 1 (STOML1, Accession NM\_004809). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STOML1. Synaptotagmin XIII (SYT13, Accession XM\_167880) is another VGAM1958 host target gene. SYT13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of SYT13 BINDING SITE, designated SEQ ID:44891, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67140] Another function of VGAM1958 is therefore inhibition of Synaptotagmin XIII (SYT13, Accession XM\_167880). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYT13. TA-PP2C (Accession NM\_139283) is another VGAM1958 host target gene. TA-PP2C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TA-PP2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TA-PP2C BINDING SITE, designated SEQ ID:29282, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67141] Another function of VGAM1958 is therefore inhibition of TA-PP2C (Accession NM\_139283). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TA-PP2C. TBC1 Domain Family, Member 2 (TBC1D2, Acces-

sion NM\_018421) is another VGAM1958 host target gene. TBC1D2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TBC1D2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBC1D2 BINDING SITE, designated SEQ ID:20468, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67142] Another function of VGAM1958 is therefore inhibition of TBC1 Domain Family, Member 2 (TBC1D2, Accession NM\_018421). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBC1D2. T-cell Leukemia/lymphoma 6 (TCL6, Accession NM\_012468) is another VGAM1958 host target gene. TCL6 BINDING SITE1 through TCL6 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCL6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCL6 BINDING SITE1 through TCL6 BINDING



SITE6, designated SEQ ID:14842, SEQ ID:14844, SEQ ID:21759, SEQ ID:21768, SEQ ID:15765 and SEQ ID:15768 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67143] Another function of VGAM1958 is therefore inhibition of T-cell Leukemia/lymphoma 6 (TCL6, Accession NM\_012468). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCL6. TIP-1 (Accession NM\_014604) is another VGAM1958 host target gene. TIP-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIP-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIP-1 BINDING SITE, designated SEQ ID:15969, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67144] Another function of VGAM1958 is therefore inhibition of TIP-1 (Accession NM\_014604). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIP-1.

Torsin Family 2, Member A (TOR2A, Accession NM\_130459) is another VGAM1958 host target gene. TOR2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOR2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOR2A BINDING SITE, designated SEQ ID:28217, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67145] Another function of VGAM1958 is therefore inhibition of Torsin Family 2, Member A (TOR2A, Accession NM\_130459). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOR2A. TNF Receptor-associated Factor 3 (TRAF3, Accession XM\_007256) is another VGAM1958 host target gene. TRAF3 BINDING SITE1 through TRAF3 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRAF3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of TRAF3 BINDING SITE1 through TRAF3 BINDING SITE4, designated SEQ ID:30046, SEQ ID:30047, SEQ ID:30049 and SEQ ID:9303 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67146] Another function of VGAM1958 is therefore inhibition of TNF Receptor-associated Factor 3 (TRAF3, Accession XM\_007256). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF3. Three Prime Repair Exonuclease 1 (TREX1, Accession NM\_033627) is another VGAM1958 host target gene. TREX1 BINDING SITE1 through TREX1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TREX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TREX1 BINDING SITE1 through TREX1 BINDING SITE3, designated SEQ ID:27342, SEQ ID:27349 and SEQ ID:13195 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67147] Another function of VGAM1958 is therefore inhibition of

Three Prime Repair Exonuclease 1 (TREX1, Accession NM\_033627). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TREX1. Tetratricopeptide Repeat Domain 4 (TTC4, Accession XM\_038926) is another VGAM1958 host target gene. TTC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TTC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTC4 BINDING SITE, designated SEQ ID:32958, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67148] Another function of VGAM1958 is therefore inhibition of Tetratricopeptide Repeat Domain 4 (TTC4, Accession XM\_038926). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTC4. Testis-specific Transcript, Y-linked 2 (TTY2, Accession XM\_099029) is another VGAM1958 host target gene. TTY2 BINDING SITE1 and TTY2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

TTTY2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTTY2 BINDING SITE1 and TTTY2 BINDING SITE2, designated SEQ ID:42069 and SEQ ID:42073 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67149] Another function of VGAM1958 is therefore inhibition of Testis-specific Transcript, Y-linked 2 (TTTY2, Accession XM\_099029). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTTY2. U5-116KD (Accession NM\_004247) is another VGAM1958 host target gene. U5-116KD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by U5-116KD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of U5-116KD BINDING SITE, designated SEQ ID:10439, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67150] Another function of VGAM1958 is therefore inhibition of U5-116KD (Accession NM\_004247). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with U5-116KD. UBAP (Accession XM\_084277) is another VGAM1958 host target gene. UBAP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by UBAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBAP BINDING SITE, designated SEQ ID:37535, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67151] Another function of VGAM1958 is therefore inhibition of UBAP (Accession XM\_084277). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBAP. Ubiquitin-like, Containing PHD and RING Finger Domains, 1 (UHRF1, Accession NM\_013282) is another VGAM1958 host target gene. UHRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UHRF1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UHRF1 BINDING SITE, designated SEQ ID:14952, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67152] Another function of VGAM1958 is therefore inhibition of Ubiquitin-like, Containing PHD and RING Finger Domains, 1 (UHRF1, Accession NM\_013282). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UHRF1. VI (Accession NM\_013443) is another VGAM1958 host target gene. VI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VI BINDING SITE, designated SEQ ID:15105, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67153] Another function of VGAM1958 is therefore inhibition of VI (Accession NM\_013443). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with VI. VMP1 (Accession NM\_030938) is another VGAM1958 host target gene. VMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VMP1 BINDING SITE, designated SEQ ID:25205, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67154] Another function of VGAM1958 is therefore inhibition of VMP1 (Accession NM\_030938). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VMP1. VPS39 (Accession XM\_031720) is another VGAM1958 host target gene. VPS39 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VPS39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VPS39 BINDING SITE, designated SEQ ID:31473, to the nucleotide sequence of VGAM1958 RNA,



herein designated VGAM RNA, also designated SEQ ID:4669.

[67155] Another function of VGAM1958 is therefore inhibition of VPS39 (Accession XM\_031720). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VPS39. WD Repeat Domain 5B (WDR5B, Accession NM\_019069) is another VGAM1958 host target gene. WDR5B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by WDR5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WDR5B BINDING SITE, designated SEQ ID:21148, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67156] Another function of VGAM1958 is therefore inhibition of WD Repeat Domain 5B (WDR5B, Accession NM\_019069). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WDR5B. Zinc Finger, DHHC Domain Containing 1 (ZDHHC1, Accession XM\_085369) is another VGAM1958 host target gene. ZDHHC1 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZDHHC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC1 BINDING SITE, designated SEQ ID:38079, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67157] Another function of VGAM1958 is therefore inhibition of Zinc Finger, DHHC Domain Containing 1 (ZDHHC1, Accession XM\_085369). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC1. Zinc Finger, DHHC Domain Containing 3 (ZDHHC3, Accession NM\_016598) is another VGAM1958 host target gene. ZDHHC3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZDHHC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC3 BINDING SITE, designated SEQ ID:18686, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ

ID:4669.

[67158] Another function of VGAM1958 is therefore inhibition of Zinc Finger, DHHC Domain Containing 3 (ZDHHC3, Accession NM\_016598). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC3. ZF (Accession NM\_021212) is another VGAM1958 host target gene. ZF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZF BINDING SITE, designated SEQ ID:22188, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67159] Another function of VGAM1958 is therefore inhibition of ZF (Accession NM\_021212). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZF. ZFD25 (Accession NM\_016220) is another VGAM1958 host target gene. ZFD25 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZFD25, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFD25 BINDING SITE, designated SEQ ID:18323, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67160] Another function of VGAM1958 is therefore inhibition of ZFD25 (Accession NM\_016220). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFD25. Zinc Finger Protein 95 Homolog (mouse) (ZFP95, Accession NM\_014569) is another VGAM1958 host target gene. ZFP95 BINDING SITE1 and ZFP95 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ZFP95, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP95 BINDING SITE1 and ZFP95 BINDING SITE2, designated SEQ ID:15922 and SEQ ID:29712 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67161] Another function of VGAM1958 is therefore inhibition of

Zinc Finger Protein 95 Homolog (mouse) (ZFP95, Accession NM\_014569). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP95. Zinc Finger Protein 197 (ZNF197, Accession NM\_006991) is another VGAM1958 host target gene. ZNF197 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF197 BINDING SITE, designated SEQ ID:13854, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67162] Another function of VGAM1958 is therefore inhibition of Zinc Finger Protein 197 (ZNF197, Accession NM\_006991). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF197. Zinc Finger Protein 213 (ZNF213, Accession XM\_036493) is another VGAM1958 host target gene. ZNF213 BINDING SITE1 and ZNF213 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ZNF213, corre-

sponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF213 BINDING SITE1 and ZNF213 BINDING SITE2, designated SEQ ID:32462 and SEQ ID:32464 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67163] Another function of VGAM1958 is therefore inhibition of Zinc Finger Protein 213 (ZNF213, Accession XM\_036493). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF213. ZNF340 (Accession XM\_097701) is another VGAM1958 host target gene. ZNF340 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF340 BINDING SITE, designated SEQ ID:41034, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67164] Another function of VGAM1958 is therefore inhibition of

ZNF340 (Accession XM\_097701). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF340. LOC114987 (Accession NM\_145241) is another VGAM1958 host target gene. LOC114987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC114987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114987 BINDING SITE, designated SEQ ID:29755, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67165] Another function of VGAM1958 is therefore inhibition of LOC114987 (Accession NM\_145241). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114987. LOC115123 (Accession XM\_055276) is another VGAM1958 host target gene. LOC115123 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC115123 BINDING SITE, designated SEQ ID:36247, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67166] Another function of VGAM1958 is therefore inhibition of LOC115123 (Accession XM\_055276). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115123. LOC121642 (Accession XM\_058581) is another VGAM1958 host target gene. LOC121642 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC121642, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121642 BINDING SITE, designated SEQ ID:36674, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67167] Another function of VGAM1958 is therefore inhibition of LOC121642 (Accession XM\_058581). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121642. LOC122416 (Accession XM\_058615) is an-



other VGAM1958 host target gene. LOC122416 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC122416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122416 BINDING SITE, designated SEQ ID:36682, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67168] Another function of VGAM1958 is therefore inhibition of LOC122416 (Accession XM\_058615). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122416. LOC122525 (Accession XM\_071793) is another VGAM1958 host target gene. LOC122525 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC122525, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122525 BINDING SITE, designated SEQ ID:37422, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67169] Another function of VGAM1958 is therefore inhibition of LOC122525 (Accession XM\_071793). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122525. LOC124044 (Accession XM\_071871) is another VGAM1958 host target gene. LOC124044 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124044, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124044 BINDING SITE, designated SEQ ID:37433, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67170] Another function of VGAM1958 is therefore inhibition of LOC124044 (Accession XM\_071871). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124044. LOC124460 (Accession XM\_071892) is another VGAM1958 host target gene. LOC124460 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC124460, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124460 BINDING SITE, designated SEQ ID:37444, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67171] Another function of VGAM1958 is therefore inhibition of LOC124460 (Accession XM\_071892). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124460. LOC126917 (Accession XM\_059091) is another VGAM1958 host target gene. LOC126917 BINDING SITE1 and LOC126917 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC126917, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126917 BINDING SITE1 and LOC126917 BINDING SITE2, designated SEQ ID:36866 and SEQ ID:36872 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67172] Another function of VGAM1958 is therefore inhibition of LOC126917 (Accession XM\_059091). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126917. LOC132332 (Accession XM\_072306) is another VGAM1958 host target gene. LOC132332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC132332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132332 BINDING SITE, designated SEQ ID:37487, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67173] Another function of VGAM1958 is therefore inhibition of LOC132332 (Accession XM\_072306). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132332. LOC133634 (Accession XM\_059664) is another VGAM1958 host target gene. LOC133634 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC133634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC133634 BINDING SITE, designated SEQ ID:37049, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67174] Another function of VGAM1958 is therefore inhibition of LOC133634 (Accession XM\_059664). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133634. LOC135398 (Accession XM\_069333) is another VGAM1958 host target gene. LOC135398 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135398, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135398 BINDING SITE, designated SEQ ID:37386, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67175] Another function of VGAM1958 is therefore inhibition of LOC135398 (Accession XM\_069333). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135398. LOC135763 (Accession NM\_138572) is another VGAM1958 host target gene. LOC135763 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135763 BINDING SITE, designated SEQ ID:28883, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67176] Another function of VGAM1958 is therefore inhibition of LOC135763 (Accession NM\_138572). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135763. LOC138617 (Accession XM\_070997) is another VGAM1958 host target gene. LOC138617 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC138617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138617 BINDING SITE, designated SEQ ID:37396, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67177] Another function of VGAM1958 is therefore inhibition of

LOC138617 (Accession XM\_070997). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138617. LOC142927 (Accession XM\_084380) is another VGAM1958 host target gene. LOC142927 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC142927, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142927 BINDING SITE, designated SEQ ID:37565, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67178] Another function of VGAM1958 is therefore inhibition of LOC142927 (Accession XM\_084380). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142927. LOC143381 (Accession XM\_084501) is another VGAM1958 host target gene. LOC143381 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143381, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC143381 BINDING SITE, designated SEQ ID:37611, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67179] Another function of VGAM1958 is therefore inhibition of LOC143381 (Accession XM\_084501). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143381. LOC143914 (Accession XM\_084654) is another VGAM1958 host target gene. LOC143914 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143914, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143914 BINDING SITE, designated SEQ ID:37636, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67180] Another function of VGAM1958 is therefore inhibition of LOC143914 (Accession XM\_084654). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143914. LOC144305 (Accession XM\_096572) is an-



other VGAM1958 host target gene. LOC144305 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144305 BINDING SITE, designated SEQ ID:40400, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67181] Another function of VGAM1958 is therefore inhibition of LOC144305 (Accession XM\_096572). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144305. LOC144373 (Accession XM\_084841) is another VGAM1958 host target gene. LOC144373 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144373 BINDING SITE, designated SEQ ID:37729, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67182] Another function of VGAM1958 is therefore inhibition of LOC144373 (Accession XM\_084841). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144373. LOC144577 (Accession XM\_084911) is another VGAM1958 host target gene. LOC144577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144577 BINDING SITE, designated SEQ ID:37768, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67183] Another function of VGAM1958 is therefore inhibition of LOC144577 (Accession XM\_084911). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144577. LOC144893 (Accession XM\_096687) is another VGAM1958 host target gene. LOC144893 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144893, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144893 BINDING SITE, designated SEQ ID:40457, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67184] Another function of VGAM1958 is therefore inhibition of LOC144893 (Accession XM\_096687). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144893. LOC145195 (Accession XM\_096731) is another VGAM1958 host target gene. LOC145195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145195 BINDING SITE, designated SEQ ID:40515, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67185] Another function of VGAM1958 is therefore inhibition of LOC145195 (Accession XM\_096731). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC145195. LOC145438 (Accession XM\_096781) is another VGAM1958 host target gene. LOC145438 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145438 BINDING SITE, designated SEQ ID:40536, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67186] Another function of VGAM1958 is therefore inhibition of LOC145438 (Accession XM\_096781). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145438. LOC145608 (Accession XM\_096818) is another VGAM1958 host target gene. LOC145608 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145608, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145608 BINDING SITE, designated SEQ ID:40541, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[67187] Another function of VGAM1958 is therefore inhibition of LOC145608 (Accession XM\_096818). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145608. LOC145678 (Accession XM\_096832) is another VGAM1958 host target gene. LOC145678 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145678 BINDING SITE, designated SEQ ID:40552, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67188] Another function of VGAM1958 is therefore inhibition of LOC145678 (Accession XM\_096832). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145678. LOC145815 (Accession XM\_096874) is another VGAM1958 host target gene. LOC145815 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145815, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145815 BINDING SITE, designated SEQ ID:40600, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67189] Another function of VGAM1958 is therefore inhibition of LOC145815 (Accession XM\_096874). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145815. LOC145820 (Accession XM\_085246) is another VGAM1958 host target gene. LOC145820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145820 BINDING SITE, designated SEQ ID:37990, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67190] Another function of VGAM1958 is therefore inhibition of LOC145820 (Accession XM\_085246). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC145820. LOC145826 (Accession XM\_096875) is another VGAM1958 host target gene. LOC145826 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145826 BINDING SITE, designated SEQ ID:40609, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67191] Another function of VGAM1958 is therefore inhibition of LOC145826 (Accession XM\_096875). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145826. LOC145989 (Accession XM\_004815) is another VGAM1958 host target gene. LOC145989 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145989 BINDING SITE, designated SEQ ID:29953, to

the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67192] Another function of VGAM1958 is therefore inhibition of LOC145989 (Accession XM\_004815). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145989. LOC146050 (Accession XM\_085301) is another VGAM1958 host target gene. LOC146050 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146050, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146050 BINDING SITE, designated SEQ ID:38057, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67193] Another function of VGAM1958 is therefore inhibition of LOC146050 (Accession XM\_085301). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146050. LOC146108 (Accession XM\_085322) is another VGAM1958 host target gene. LOC146108 BINDING SITE1 and LOC146108 BINDING SITE2 are HOST TARGET



binding sites found in untranslated regions of mRNA encoded by LOC146108, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146108 BINDING SITE1 and LOC146108 BINDING SITE2, designated SEQ ID:38059 and SEQ ID:38060 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67194] Another function of VGAM1958 is therefore inhibition of LOC146108 (Accession XM\_085322). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146108. LOC146445 (Accession XM\_096999) is another VGAM1958 host target gene. LOC146445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146445 BINDING SITE, designated SEQ ID:40698, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67195] Another function of VGAM1958 is therefore inhibition of LOC146445 (Accession XM\_096999). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146445. LOC146455 (Accession XM\_085471) is another VGAM1958 host target gene. LOC146455 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146455, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146455 BINDING SITE, designated SEQ ID:38158, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67196] Another function of VGAM1958 is therefore inhibition of LOC146455 (Accession XM\_085471). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146455. LOC146488 (Accession XM\_047748) is another VGAM1958 host target gene. LOC146488 BINDING SITE1 through LOC146488 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC146488, corresponding to HOST TARGET

binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146488 BINDING SITE1 through LOC146488 BINDING SITE3, designated SEQ ID:35047, SEQ ID:35048 and SEQ ID:35049 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67197] Another function of VGAM1958 is therefore inhibition of LOC146488 (Accession XM\_047748). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146488. LOC146669 (Accession XM\_085534) is another VGAM1958 host target gene. LOC146669 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146669 BINDING SITE, designated SEQ ID:38225, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67198] Another function of VGAM1958 is therefore inhibition of LOC146669 (Accession XM\_085534). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146669. LOC146756 (Accession XM\_097085) is another VGAM1958 host target gene. LOC146756 BINDING SITE1 and LOC146756 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC146756, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146756 BINDING SITE1 and LOC146756 BINDING SITE2, designated SEQ ID:40735 and SEQ ID:40738 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67199] Another function of VGAM1958 is therefore inhibition of LOC146756 (Accession XM\_097085). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146756. LOC146839 (Accession XM\_097107) is another VGAM1958 host target gene. LOC146839 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146839, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146839 BINDING SITE, designated SEQ ID:40756, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67200] Another function of VGAM1958 is therefore inhibition of LOC146839 (Accession XM\_097107). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146839. LOC146990 (Accession XM\_097149) is another VGAM1958 host target gene. LOC146990 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146990, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146990 BINDING SITE, designated SEQ ID:40776, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67201] Another function of VGAM1958 is therefore inhibition of LOC146990 (Accession XM\_097149). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC146990. LOC147054 (Accession XM\_097172) is another VGAM1958 host target gene. LOC147054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147054 BINDING SITE, designated SEQ ID:40794, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67202] Another function of VGAM1958 is therefore inhibition of LOC147054 (Accession XM\_097172). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147054. LOC147057 (Accession XM\_097166) is another VGAM1958 host target gene. LOC147057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147057 BINDING SITE, designated SEQ ID:40784, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[67203] Another function of VGAM1958 is therefore inhibition of LOC147057 (Accession XM\_097166). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147057. LOC147077 (Accession XM\_085699) is another VGAM1958 host target gene. LOC147077 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147077 BINDING SITE, designated SEQ ID:38297, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67204] Another function of VGAM1958 is therefore inhibition of LOC147077 (Accession XM\_085699). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147077. LOC147136 (Accession XM\_085716) is another VGAM1958 host target gene. LOC147136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147136, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147136 BINDING SITE, designated SEQ ID:38305, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67205] Another function of VGAM1958 is therefore inhibition of LOC147136 (Accession XM\_085716). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147136. LOC147160 (Accession XM\_097202) is another VGAM1958 host target gene. LOC147160 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147160 BINDING SITE, designated SEQ ID:40810, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67206] Another function of VGAM1958 is therefore inhibition of LOC147160 (Accession XM\_097202). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC147160. LOC147353 (Accession XM\_097227) is another VGAM1958 host target gene. LOC147353 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147353, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147353 BINDING SITE, designated SEQ ID:40833, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67207] Another function of VGAM1958 is therefore inhibition of LOC147353 (Accession XM\_097227). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147353. LOC148114 (Accession XM\_086050) is another VGAM1958 host target gene. LOC148114 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148114 BINDING SITE, designated SEQ ID:38467, to

the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67208] Another function of VGAM1958 is therefore inhibition of LOC148114 (Accession XM\_086050). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148114. LOC148479 (Accession XM\_086204) is another VGAM1958 host target gene. LOC148479 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148479 BINDING SITE, designated SEQ ID:38542, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67209] Another function of VGAM1958 is therefore inhibition of LOC148479 (Accession XM\_086204). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148479. LOC148603 (Accession XM\_086247) is another VGAM1958 host target gene. LOC148603 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC148603, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148603 BINDING SITE, designated SEQ ID:38568, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67210] Another function of VGAM1958 is therefore inhibition of LOC148603 (Accession XM\_086247). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148603. LOC148697 (Accession XM\_086276) is another VGAM1958 host target gene. LOC148697 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148697, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148697 BINDING SITE, designated SEQ ID:38570, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67211] Another function of VGAM1958 is therefore inhibition of LOC148697 (Accession XM\_086276). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148697. LOC148809 (Accession XM\_086325) is another VGAM1958 host target gene. LOC148809 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148809, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148809 BINDING SITE, designated SEQ ID:38592, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67212] Another function of VGAM1958 is therefore inhibition of LOC148809 (Accession XM\_086325). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148809. LOC148894 (Accession XM\_097542) is another VGAM1958 host target gene. LOC148894 BINDING SITE1 and LOC148894 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC148894, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LOC148894 BINDING SITE1 and LOC148894 BINDING SITE2, designated SEQ ID:40915 and SEQ ID:40918 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67213] Another function of VGAM1958 is therefore inhibition of LOC148894 (Accession XM\_097542). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148894. LOC149271 (Accession XM\_086475) is another VGAM1958 host target gene. LOC149271 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149271 BINDING SITE, designated SEQ ID:38680, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67214] Another function of VGAM1958 is therefore inhibition of LOC149271 (Accession XM\_086475). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC149271. LOC149332 (Accession XM\_097626) is another VGAM1958 host target gene. LOC149332 BINDING SITE1 and LOC149332 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC149332, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149332 BINDING SITE1 and LOC149332 BINDING SITE2, designated SEQ ID:40980 and SEQ ID:40981 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67215] Another function of VGAM1958 is therefore inhibition of LOC149332 (Accession XM\_097626). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149332. LOC149421 (Accession XM\_086528) is another VGAM1958 host target gene. LOC149421 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149421, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC149421 BINDING SITE, designated SEQ ID:38745, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67216] Another function of VGAM1958 is therefore inhibition of LOC149421 (Accession XM\_086528). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149421. LOC149501 (Accession XM\_059930) is another VGAM1958 host target gene. LOC149501 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149501 BINDING SITE, designated SEQ ID:37108, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67217] Another function of VGAM1958 is therefore inhibition of LOC149501 (Accession XM\_059930). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149501. LOC149684 (Accession XM\_097710) is another VGAM1958 host target gene. LOC149684 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149684, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149684 BINDING SITE, designated SEQ ID:41047, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67218] Another function of VGAM1958 is therefore inhibition of LOC149684 (Accession XM\_097710). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149684. LOC149773 (Accession XM\_086628) is another VGAM1958 host target gene. LOC149773 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149773 BINDING SITE, designated SEQ ID:38800, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67219] Another function of VGAM1958 is therefore inhibition of



LOC149773 (Accession XM\_086628). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149773. LOC149950 (Accession XM\_086732) is another VGAM1958 host target gene. LOC149950 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149950 BINDING SITE, designated SEQ ID:38840, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67220] Another function of VGAM1958 is therefore inhibition of LOC149950 (Accession XM\_086732). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149950. LOC150135 (Accession XM\_086785) is another VGAM1958 host target gene. LOC150135 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150135, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC150135 BINDING SITE, designated SEQ ID:38846, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67221] Another function of VGAM1958 is therefore inhibition of LOC150135 (Accession XM\_086785). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150135. LOC150139 (Accession XM\_086794) is another VGAM1958 host target gene. LOC150139 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150139 BINDING SITE, designated SEQ ID:38857, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67222] Another function of VGAM1958 is therefore inhibition of LOC150139 (Accession XM\_086794). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150139. LOC150150 (Accession XM\_097820) is an-

other VGAM1958 host target gene. LOC150150 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150150, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150150 BINDING SITE, designated SEQ ID:41133, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67223] Another function of VGAM1958 is therefore inhibition of LOC150150 (Accession XM\_097820). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150150. LOC150157 (Accession XM\_097823) is another VGAM1958 host target gene. LOC150157 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150157 BINDING SITE, designated SEQ ID:41140, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67224] Another function of VGAM1958 is therefore inhibition of LOC150157 (Accession XM\_097823). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150157. LOC150166 (Accession XM\_097824) is another VGAM1958 host target gene. LOC150166 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150166 BINDING SITE, designated SEQ ID:41148, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67225] Another function of VGAM1958 is therefore inhibition of LOC150166 (Accession XM\_097824). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150166. LOC150406 (Accession XM\_086908) is another VGAM1958 host target gene. LOC150406 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150406, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150406 BINDING SITE, designated SEQ ID:38964, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67226] Another function of VGAM1958 is therefore inhibition of LOC150406 (Accession XM\_086908). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150406. LOC150445 (Accession XM\_086916) is another VGAM1958 host target gene. LOC150445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150445 BINDING SITE, designated SEQ ID:38971, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67227] Another function of VGAM1958 is therefore inhibition of LOC150445 (Accession XM\_086916). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC150445. LOC150465 (Accession XM\_086924) is another VGAM1958 host target gene. LOC150465 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150465 BINDING SITE, designated SEQ ID:38973, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67228] Another function of VGAM1958 is therefore inhibition of LOC150465 (Accession XM\_086924). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150465. LOC150568 (Accession XM\_097911) is another VGAM1958 host target gene. LOC150568 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150568 BINDING SITE, designated SEQ ID:41205, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[67229] Another function of VGAM1958 is therefore inhibition of LOC150568 (Accession XM\_097911). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150568. LOC150577 (Accession XM\_097918) is another VGAM1958 host target gene. LOC150577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150577 BINDING SITE, designated SEQ ID:41215, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67230] Another function of VGAM1958 is therefore inhibition of LOC150577 (Accession XM\_097918). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150577. LOC150587 (Accession XM\_097917) is another VGAM1958 host target gene. LOC150587 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150587, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150587 BINDING SITE, designated SEQ ID:41212, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67231] Another function of VGAM1958 is therefore inhibition of LOC150587 (Accession XM\_097917). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150587. LOC150696 (Accession NM\_144707) is another VGAM1958 host target gene. LOC150696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150696 BINDING SITE, designated SEQ ID:29529, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67232] Another function of VGAM1958 is therefore inhibition of LOC150696 (Accession NM\_144707). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC150696. LOC150837 (Accession XM\_087019) is another VGAM1958 host target gene. LOC150837 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC150837, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150837 BINDING SITE, designated SEQ ID:39015, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67233] Another function of VGAM1958 is therefore inhibition of LOC150837 (Accession XM\_087019). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150837. LOC150886 (Accession XM\_097963) is another VGAM1958 host target gene. LOC150886 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150886, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150886 BINDING SITE, designated SEQ ID:41268, to

the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67234] Another function of VGAM1958 is therefore inhibition of LOC150886 (Accession XM\_097963). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150886. LOC151361 (Accession XM\_098048) is another VGAM1958 host target gene. LOC151361 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151361 BINDING SITE, designated SEQ ID:41331, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67235] Another function of VGAM1958 is therefore inhibition of LOC151361 (Accession XM\_098048). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151361. LOC151438 (Accession XM\_098060) is another VGAM1958 host target gene. LOC151438 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC151438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151438 BINDING SITE, designated SEQ ID:41349, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67236] Another function of VGAM1958 is therefore inhibition of LOC151438 (Accession XM\_098060). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151438. LOC151457 (Accession XM\_087203) is another VGAM1958 host target gene. LOC151457 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151457, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151457 BINDING SITE, designated SEQ ID:39116, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67237] Another function of VGAM1958 is therefore inhibition of LOC151457 (Accession XM\_087203). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151457. LOC151568 (Accession NM\_138483) is another VGAM1958 host target gene. LOC151568 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151568 BINDING SITE, designated SEQ ID:28838, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67238] Another function of VGAM1958 is therefore inhibition of LOC151568 (Accession NM\_138483). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151568. LOC151647 (Accession XM\_087261) is another VGAM1958 host target gene. LOC151647 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151647, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC151647 BINDING SITE, designated SEQ ID:39158, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67239] Another function of VGAM1958 is therefore inhibition of LOC151647 (Accession XM\_087261). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151647. LOC152286 (Accession XM\_098188) is another VGAM1958 host target gene. LOC152286 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152286 BINDING SITE, designated SEQ ID:41462, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67240] Another function of VGAM1958 is therefore inhibition of LOC152286 (Accession XM\_098188). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152286. LOC152317 (Accession XM\_098189) is another VGAM1958 host target gene. LOC152317 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152317 BINDING SITE, designated SEQ ID:41464, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67241] Another function of VGAM1958 is therefore inhibition of LOC152317 (Accession XM\_098189). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152317. LOC152343 (Accession XM\_087441) is another VGAM1958 host target gene. LOC152343 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152343, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152343 BINDING SITE, designated SEQ ID:39260, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67242] Another function of VGAM1958 is therefore inhibition of

LOC152343 (Accession XM\_087441). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152343. LOC152426 (Accession XM\_098225) is another VGAM1958 host target gene. LOC152426 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152426 BINDING SITE, designated SEQ ID:41500, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67243] Another function of VGAM1958 is therefore inhibition of LOC152426 (Accession XM\_098225). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152426. LOC152441 (Accession XM\_098230) is another VGAM1958 host target gene. LOC152441 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC152441 BINDING SITE, designated SEQ ID:41506, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67244] Another function of VGAM1958 is therefore inhibition of LOC152441 (Accession XM\_098230). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152441. LOC152453 (Accession XM\_087475) is another VGAM1958 host target gene. LOC152453 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152453 BINDING SITE, designated SEQ ID:39277, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67245] Another function of VGAM1958 is therefore inhibition of LOC152453 (Accession XM\_087475). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152453. LOC152667 (Accession XM\_087500) is an-



other VGAM1958 host target gene. LOC152667 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152667, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152667 BINDING SITE, designated SEQ ID:39300, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67246] Another function of VGAM1958 is therefore inhibition of LOC152667 (Accession XM\_087500). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152667. LOC152926 (Accession XM\_087562) is another VGAM1958 host target gene. LOC152926 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152926, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152926 BINDING SITE, designated SEQ ID:39342, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67247] Another function of VGAM1958 is therefore inhibition of LOC152926 (Accession XM\_087562). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152926. LOC152992 (Accession XM\_087575) is another VGAM1958 host target gene. LOC152992 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152992 BINDING SITE, designated SEQ ID:39350, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67248] Another function of VGAM1958 is therefore inhibition of LOC152992 (Accession XM\_087575). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152992. LOC153505 (Accession XM\_087693) is another VGAM1958 host target gene. LOC153505 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153505, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153505 BINDING SITE, designated SEQ ID:39381, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67249] Another function of VGAM1958 is therefore inhibition of LOC153505 (Accession XM\_087693). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153505. LOC153811 (Accession XM\_087779) is another VGAM1958 host target gene. LOC153811 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153811 BINDING SITE, designated SEQ ID:39417, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67250] Another function of VGAM1958 is therefore inhibition of LOC153811 (Accession XM\_087779). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC153811. LOC153914 (Accession XM\_087799) is another VGAM1958 host target gene. LOC153914 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153914, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153914 BINDING SITE, designated SEQ ID:39434, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67251] Another function of VGAM1958 is therefore inhibition of LOC153914 (Accession XM\_087799). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153914. LOC154007 (Accession XM\_087824) is another VGAM1958 host target gene. LOC154007 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154007 BINDING SITE, designated SEQ ID:39452, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[67252] Another function of VGAM1958 is therefore inhibition of LOC154007 (Accession XM\_087824). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154007. LOC154222 (Accession XM\_098497) is another VGAM1958 host target gene. LOC154222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154222 BINDING SITE, designated SEQ ID:41691, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67253] Another function of VGAM1958 is therefore inhibition of LOC154222 (Accession XM\_098497). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154222. LOC154739 (Accession XM\_098602) is another VGAM1958 host target gene. LOC154739 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154739, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154739 BINDING SITE, designated SEQ ID:41718, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67254] Another function of VGAM1958 is therefore inhibition of LOC154739 (Accession XM\_098602). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154739. LOC154877 (Accession XM\_098626) is another VGAM1958 host target gene. LOC154877 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154877 BINDING SITE, designated SEQ ID:41741, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67255] Another function of VGAM1958 is therefore inhibition of LOC154877 (Accession XM\_098626). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC154877. LOC155006 (Accession XM\_088117) is another VGAM1958 host target gene. LOC155006 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155006, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155006 BINDING SITE, designated SEQ ID:39525, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67256] Another function of VGAM1958 is therefore inhibition of LOC155006 (Accession XM\_088117). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155006. LOC155036 (Accession XM\_098651) is another VGAM1958 host target gene. LOC155036 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC155036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155036 BINDING SITE, designated SEQ ID:41754, to

the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67257] Another function of VGAM1958 is therefore inhibition of LOC155036 (Accession XM\_098651). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155036. LOC155434 (Accession XM\_098723) is another VGAM1958 host target gene. LOC155434 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155434 BINDING SITE, designated SEQ ID:41772, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67258] Another function of VGAM1958 is therefore inhibition of LOC155434 (Accession XM\_098723). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155434. LOC155435 (Accession XM\_088257) is another VGAM1958 host target gene. LOC155435 BINDING SITE is HOST TARGET binding site found in the 3' un-



translated region of mRNA encoded by LOC155435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155435 BINDING SITE, designated SEQ ID:39570, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67259] Another function of VGAM1958 is therefore inhibition of LOC155435 (Accession XM\_088257). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155435. LOC157273 (Accession XM\_098743) is another VGAM1958 host target gene. LOC157273 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157273 BINDING SITE, designated SEQ ID:41779, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67260] Another function of VGAM1958 is therefore inhibition of LOC157273 (Accession XM\_098743). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157273. LOC157556 (Accession XM\_098783) is another VGAM1958 host target gene. LOC157556 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157556 BINDING SITE, designated SEQ ID:41820, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67261] Another function of VGAM1958 is therefore inhibition of LOC157556 (Accession XM\_098783). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157556. LOC157623 (Accession XM\_088346) is another VGAM1958 host target gene. LOC157623 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157623, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC157623 BINDING SITE, designated SEQ ID:39616, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67262] Another function of VGAM1958 is therefore inhibition of LOC157623 (Accession XM\_088346). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157623. LOC157753 (Accession XM\_088381) is another VGAM1958 host target gene. LOC157753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157753 BINDING SITE, designated SEQ ID:39660, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67263] Another function of VGAM1958 is therefore inhibition of LOC157753 (Accession XM\_088381). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157753. LOC157860 (Accession XM\_098832) is another VGAM1958 host target gene. LOC157860 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157860 BINDING SITE, designated SEQ ID:41858, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67264] Another function of VGAM1958 is therefore inhibition of LOC157860 (Accession XM\_098832). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157860. LOC157922 (Accession XM\_098841) is another VGAM1958 host target gene. LOC157922 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157922 BINDING SITE, designated SEQ ID:41888, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67265] Another function of VGAM1958 is therefore inhibition of

LOC157922 (Accession XM\_098841). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157922. LOC157927 (Accession XM\_098848) is another VGAM1958 host target gene. LOC157927 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157927, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157927 BINDING SITE, designated SEQ ID:41907, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67266] Another function of VGAM1958 is therefore inhibition of LOC157927 (Accession XM\_098848). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157927. LOC158046 (Accession NM\_145283) is another VGAM1958 host target gene. LOC158046 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC158046 BINDING SITE, designated SEQ ID:29800, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67267] Another function of VGAM1958 is therefore inhibition of LOC158046 (Accession NM\_145283). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158046. LOC158308 (Accession XM\_098917) is another VGAM1958 host target gene. LOC158308 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158308 BINDING SITE, designated SEQ ID:41940, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67268] Another function of VGAM1958 is therefore inhibition of LOC158308 (Accession XM\_098917). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158308. LOC158310 (Accession XM\_098919) is an-

other VGAM1958 host target gene. LOC158310 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158310 BINDING SITE, designated SEQ ID:41947, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67269] Another function of VGAM1958 is therefore inhibition of LOC158310 (Accession XM\_098919). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158310. LOC158427 (Accession NM\_139246) is another VGAM1958 host target gene. LOC158427 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158427 BINDING SITE, designated SEQ ID:29247, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67270] Another function of VGAM1958 is therefore inhibition of LOC158427 (Accession NM\_139246). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158427. LOC158563 (Accession XM\_088606) is another VGAM1958 host target gene. LOC158563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158563 BINDING SITE, designated SEQ ID:39870, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67271] Another function of VGAM1958 is therefore inhibition of LOC158563 (Accession XM\_088606). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158563. LOC158856 (Accession XM\_098998) is another VGAM1958 host target gene. LOC158856 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158856, corresponding to a HOST TARGET binding site such as BIND-



ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158856 BINDING SITE, designated SEQ ID:42034, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67272] Another function of VGAM1958 is therefore inhibition of LOC158856 (Accession XM\_098998). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158856. LOC158969 (Accession XM\_088728) is another VGAM1958 host target gene. LOC158969 BINDING SITE1 and LOC158969 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC158969, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158969 BINDING SITE1 and LOC158969 BINDING SITE2, designated SEQ ID:39918 and SEQ ID:39920 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67273] Another function of VGAM1958 is therefore inhibition of LOC158969 (Accession XM\_088728). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158969. LOC159148 (Accession XM\_099030) is another VGAM1958 host target gene. LOC159148 BINDING SITE1 and LOC159148 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC159148, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159148 BINDING SITE1 and LOC159148 BINDING SITE2, designated SEQ ID:42080 and SEQ ID:39978 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67274] Another function of VGAM1958 is therefore inhibition of LOC159148 (Accession XM\_099030). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159148. LOC161877 (Accession XM\_091190) is another VGAM1958 host target gene. LOC161877 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC161877, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161877 BINDING SITE, designated SEQ ID:40042, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67275] Another function of VGAM1958 is therefore inhibition of LOC161877 (Accession XM\_091190). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161877. LOC163412 (Accession XM\_088868) is another VGAM1958 host target gene. LOC163412 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163412, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163412 BINDING SITE, designated SEQ ID:39950, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67276] Another function of VGAM1958 is therefore inhibition of LOC163412 (Accession XM\_088868). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC163412. LOC165246 (Accession XM\_092473) is another VGAM1958 host target gene. LOC165246 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC165246, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165246 BINDING SITE, designated SEQ ID:40125, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67277] Another function of VGAM1958 is therefore inhibition of LOC165246 (Accession XM\_092473). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165246. LOC169225 (Accession XM\_108531) is another VGAM1958 host target gene. LOC169225 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC169225, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169225 BINDING SITE, designated SEQ ID:42204, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[67278] Another function of VGAM1958 is therefore inhibition of LOC169225 (Accession XM\_108531). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169225. LOC170425 (Accession XM\_084330) is another VGAM1958 host target gene. LOC170425 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC170425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170425 BINDING SITE, designated SEQ ID:37549, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67279] Another function of VGAM1958 is therefore inhibition of LOC170425 (Accession XM\_084330). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170425. LOC196027 (Accession XM\_113633) is another VGAM1958 host target gene. LOC196027 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196027, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196027 BINDING SITE, designated SEQ ID:42307, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67280] Another function of VGAM1958 is therefore inhibition of LOC196027 (Accession XM\_113633). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196027. LOC196205 (Accession XM\_113676) is another VGAM1958 host target gene. LOC196205 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196205 BINDING SITE, designated SEQ ID:42325, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67281] Another function of VGAM1958 is therefore inhibition of LOC196205 (Accession XM\_113676). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC196205. LOC196337 (Accession XM\_113696) is another VGAM1958 host target gene. LOC196337 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC196337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196337 BINDING SITE, designated SEQ ID:42360, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67282] Another function of VGAM1958 is therefore inhibition of LOC196337 (Accession XM\_113696). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196337. LOC196738 (Accession XM\_113588) is another VGAM1958 host target gene. LOC196738 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC196738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196738 BINDING SITE, designated SEQ ID:42287, to

the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67283] Another function of VGAM1958 is therefore inhibition of LOC196738 (Accession XM\_113588). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196738. LOC196812 (Accession XM\_116868) is another VGAM1958 host target gene. LOC196812 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196812 BINDING SITE, designated SEQ ID:43132, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67284] Another function of VGAM1958 is therefore inhibition of LOC196812 (Accession XM\_116868). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196812. LOC196955 (Accession XM\_085210) is another VGAM1958 host target gene. LOC196955 BINDING SITE is HOST TARGET binding site found in the 5' un-



translated region of mRNA encoded by LOC196955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196955 BINDING SITE, designated SEQ ID:37929, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67285] Another function of VGAM1958 is therefore inhibition of LOC196955 (Accession XM\_085210). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196955. LOC197350 (Accession XM\_113871) is another VGAM1958 host target gene. LOC197350 BINDING SITE1 and LOC197350 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC197350, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197350 BINDING SITE1 and LOC197350 BINDING SITE2, designated SEQ ID:42503 and SEQ ID:42504 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67286] Another function of VGAM1958 is therefore inhibition of LOC197350 (Accession XM\_113871). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197350. LOC199858 (Accession XM\_114040) is another VGAM1958 host target gene. LOC199858 BINDING SITE1 and LOC199858 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC199858, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199858 BINDING SITE1 and LOC199858 BINDING SITE2, designated SEQ ID:42630 and SEQ ID:42631 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67287] Another function of VGAM1958 is therefore inhibition of LOC199858 (Accession XM\_114040). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199858. LOC200325 (Accession XM\_117223) is another VGAM1958 host target gene. LOC200325 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC200325, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200325 BINDING SITE, designated SEQ ID:43289, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67288] Another function of VGAM1958 is therefore inhibition of LOC200325 (Accession XM\_117223). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200325. LOC200470 (Accession XM\_117235) is another VGAM1958 host target gene. LOC200470 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200470, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200470 BINDING SITE, designated SEQ ID:43308, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67289] Another function of VGAM1958 is therefore inhibition of LOC200470 (Accession XM\_117235). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200470. LOC200597 (Accession XM\_114266) is another VGAM1958 host target gene. LOC200597 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200597 BINDING SITE, designated SEQ ID:42824, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67290] Another function of VGAM1958 is therefore inhibition of LOC200597 (Accession XM\_114266). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200597. LOC200853 (Accession XM\_114308) is another VGAM1958 host target gene. LOC200853 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC200853 BINDING SITE, designated SEQ ID:42867, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67291] Another function of VGAM1958 is therefore inhibition of LOC200853 (Accession XM\_114308). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200853. LOC201191 (Accession XM\_117058) is another VGAM1958 host target gene. LOC201191 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201191 BINDING SITE, designated SEQ ID:43216, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67292] Another function of VGAM1958 is therefore inhibition of LOC201191 (Accession XM\_117058). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201191. LOC201627 (Accession XM\_114353) is another VGAM1958 host target gene. LOC201627 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201627 BINDING SITE, designated SEQ ID:42895, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67293] Another function of VGAM1958 is therefore inhibition of LOC201627 (Accession XM\_114353). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201627. LOC202052 (Accession XM\_117355) is another VGAM1958 host target gene. LOC202052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202052 BINDING SITE, designated SEQ ID:43407, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67294] Another function of VGAM1958 is therefore inhibition of

LOC202052 (Accession XM\_117355). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202052. LOC202451 (Accession XM\_117401) is another VGAM1958 host target gene. LOC202451 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202451 BINDING SITE, designated SEQ ID:43439, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67295] Another function of VGAM1958 is therefore inhibition of LOC202451 (Accession XM\_117401). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202451. LOC203078 (Accession XM\_114625) is another VGAM1958 host target gene. LOC203078 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC203078 BINDING SITE, designated SEQ ID:43005, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67296] Another function of VGAM1958 is therefore inhibition of LOC203078 (Accession XM\_114625). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203078. LOC203246 (Accession XM\_114658) is another VGAM1958 host target gene. LOC203246 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203246, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203246 BINDING SITE, designated SEQ ID:43015, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67297] Another function of VGAM1958 is therefore inhibition of LOC203246 (Accession XM\_114658). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203246. LOC203276 (Accession XM\_117523) is an-



other VGAM1958 host target gene. LOC203276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203276 BINDING SITE, designated SEQ ID:43484, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67298] Another function of VGAM1958 is therefore inhibition of LOC203276 (Accession XM\_117523). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203276. LOC203305 (Accession XM\_117529) is another VGAM1958 host target gene. LOC203305 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203305 BINDING SITE, designated SEQ ID:43508, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67299] Another function of VGAM1958 is therefore inhibition of LOC203305 (Accession XM\_117529). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203305. LOC203350 (Accession XM\_117536) is another VGAM1958 host target gene. LOC203350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203350 BINDING SITE, designated SEQ ID:43537, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67300] Another function of VGAM1958 is therefore inhibition of LOC203350 (Accession XM\_117536). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203350. LOC203378 (Accession XM\_117541) is another VGAM1958 host target gene. LOC203378 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203378, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203378 BINDING SITE, designated SEQ ID:43548, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67301] Another function of VGAM1958 is therefore inhibition of LOC203378 (Accession XM\_117541). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203378. LOC204161 (Accession XM\_118480) is another VGAM1958 host target gene. LOC204161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204161 BINDING SITE, designated SEQ ID:43578, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67302] Another function of VGAM1958 is therefore inhibition of LOC204161 (Accession XM\_118480). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC204161. LOC204804 (Accession XM\_115599) is another VGAM1958 host target gene. LOC204804 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204804, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204804 BINDING SITE, designated SEQ ID:43098, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67303] Another function of VGAM1958 is therefore inhibition of LOC204804 (Accession XM\_115599). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204804. LOC204970 (Accession XM\_114795) is another VGAM1958 host target gene. LOC204970 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204970 BINDING SITE, designated SEQ ID:43070, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[67304] Another function of VGAM1958 is therefore inhibition of LOC204970 (Accession XM\_114795). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204970. LOC205327 (Accession XM\_115788) is another VGAM1958 host target gene. LOC205327 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC205327, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205327 BINDING SITE, designated SEQ ID:43105, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67305] Another function of VGAM1958 is therefore inhibition of LOC205327 (Accession XM\_115788). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205327. LOC219404 (Accession XM\_167909) is another VGAM1958 host target gene. LOC219404 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219404, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219404 BINDING SITE, designated SEQ ID:44908, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67306] Another function of VGAM1958 is therefore inhibition of LOC219404 (Accession XM\_167909). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219404. LOC219686 (Accession XM\_165544) is another VGAM1958 host target gene. LOC219686 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219686, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219686 BINDING SITE, designated SEQ ID:43673, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67307] Another function of VGAM1958 is therefore inhibition of LOC219686 (Accession XM\_165544). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC219686. LOC219848 (Accession XM\_166170) is another VGAM1958 host target gene. LOC219848 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC219848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219848 BINDING SITE, designated SEQ ID:43985, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67308] Another function of VGAM1958 is therefore inhibition of LOC219848 (Accession XM\_166170). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219848. LOC219942 (Accession XM\_167790) is another VGAM1958 host target gene. LOC219942 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC219942, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219942 BINDING SITE, designated SEQ ID:44825, to

the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67309] Another function of VGAM1958 is therefore inhibition of LOC219942 (Accession XM\_167790). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219942. LOC220045 (Accession XM\_167820) is another VGAM1958 host target gene. LOC220045 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220045 BINDING SITE, designated SEQ ID:44861, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67310] Another function of VGAM1958 is therefore inhibition of LOC220045 (Accession XM\_167820). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220045. LOC220143 (Accession XM\_168046) is another VGAM1958 host target gene. LOC220143 BINDING SITE is HOST TARGET binding site found in the 3' un-



translated region of mRNA encoded by LOC220143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220143 BINDING SITE, designated SEQ ID:44953, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67311] Another function of VGAM1958 is therefore inhibition of LOC220143 (Accession XM\_168046). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220143. LOC220739 (Accession XM\_167548) is another VGAM1958 host target gene. LOC220739 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220739 BINDING SITE, designated SEQ ID:44657, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67312] Another function of VGAM1958 is therefore inhibition of LOC220739 (Accession XM\_167548). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220739. LOC220776 (Accession XM\_043388) is another VGAM1958 host target gene. LOC220776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220776 BINDING SITE, designated SEQ ID:33939, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67313] Another function of VGAM1958 is therefore inhibition of LOC220776 (Accession XM\_043388). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220776. LOC220929 (Accession XM\_166134) is another VGAM1958 host target gene. LOC220929 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220929, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC220929 BINDING SITE, designated SEQ ID:43928, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67314] Another function of VGAM1958 is therefore inhibition of LOC220929 (Accession XM\_166134). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220929. LOC221002 (Accession XM\_166156) is another VGAM1958 host target gene. LOC221002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221002 BINDING SITE, designated SEQ ID:43977, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67315] Another function of VGAM1958 is therefore inhibition of LOC221002 (Accession XM\_166156). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221002. LOC221042 (Accession XM\_167669) is another VGAM1958 host target gene. LOC221042 BINDING

SITE1 and LOC221042 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC221042, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221042 BINDING SITE1 and LOC221042 BINDING SITE2, designated SEQ ID:44753 and SEQ ID:44754 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67316] Another function of VGAM1958 is therefore inhibition of LOC221042 (Accession XM\_167669). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221042. LOC221477 (Accession XM\_166397) is another VGAM1958 host target gene. LOC221477 BINDING SITE1 and LOC221477 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC221477, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221477 BINDING SITE1 and LOC221477 BINDING SITE2, designated SEQ ID:44249

and SEQ ID:44250 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67317] Another function of VGAM1958 is therefore inhibition of LOC221477 (Accession XM\_166397). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221477. LOC221687 (Accession XM\_166423) is another VGAM1958 host target gene. LOC221687 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221687 BINDING SITE, designated SEQ ID:44304, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67318] Another function of VGAM1958 is therefore inhibition of LOC221687 (Accession XM\_166423). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221687. LOC221935 (Accession XM\_166537) is another VGAM1958 host target gene. LOC221935 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221935 BINDING SITE, designated SEQ ID:44503, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67319] Another function of VGAM1958 is therefore inhibition of LOC221935 (Accession XM\_166537). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221935. LOC222237 (Accession XM\_168592) is another VGAM1958 host target gene. LOC222237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222237 BINDING SITE, designated SEQ ID:45269, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67320] Another function of VGAM1958 is therefore inhibition of

LOC222237 (Accession XM\_168592). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222237. LOC253019 (Accession XM\_170907) is another VGAM1958 host target gene. LOC253019 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253019 BINDING SITE, designated SEQ ID:45669, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67321] Another function of VGAM1958 is therefore inhibition of LOC253019 (Accession XM\_170907). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253019. LOC253502 (Accession XM\_170561) is another VGAM1958 host target gene. LOC253502 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253502, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC253502 BINDING SITE, designated SEQ ID:45380, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67322] Another function of VGAM1958 is therefore inhibition of LOC253502 (Accession XM\_170561). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253502. LOC253664 (Accession XM\_170673) is another VGAM1958 host target gene. LOC253664 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253664, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253664 BINDING SITE, designated SEQ ID:45450, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67323] Another function of VGAM1958 is therefore inhibition of LOC253664 (Accession XM\_170673). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253664. LOC253975 (Accession XM\_171130) is an-



other VGAM1958 host target gene. LOC253975 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253975, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253975 BINDING SITE, designated SEQ ID:45936, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67324] Another function of VGAM1958 is therefore inhibition of LOC253975 (Accession XM\_171130). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253975. LOC253981 (Accession XM\_171064) is another VGAM1958 host target gene. LOC253981 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253981 BINDING SITE, designated SEQ ID:45866, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67325] Another function of VGAM1958 is therefore inhibition of LOC253981 (Accession XM\_171064). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253981. LOC254015 (Accession XM\_172977) is another VGAM1958 host target gene. LOC254015 BINDING SITE1 and LOC254015 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC254015, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254015 BINDING SITE1 and LOC254015 BINDING SITE2, designated SEQ ID:46243 and SEQ ID:46245 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67326] Another function of VGAM1958 is therefore inhibition of LOC254015 (Accession XM\_172977). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254015. LOC254243 (Accession XM\_173233) is another VGAM1958 host target gene. LOC254243 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC254243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254243 BINDING SITE, designated SEQ ID:46510, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67327] Another function of VGAM1958 is therefore inhibition of LOC254243 (Accession XM\_173233). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254243. LOC254531 (Accession XM\_170773) is another VGAM1958 host target gene. LOC254531 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254531, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254531 BINDING SITE, designated SEQ ID:45540, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67328] Another function of VGAM1958 is therefore inhibition of LOC254531 (Accession XM\_170773). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254531. LOC254532 (Accession XM\_172961) is another VGAM1958 host target gene. LOC254532 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254532 BINDING SITE, designated SEQ ID:46207, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67329] Another function of VGAM1958 is therefore inhibition of LOC254532 (Accession XM\_172961). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254532. LOC255057 (Accession XM\_170903) is another VGAM1958 host target gene. LOC255057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC255057 BINDING SITE, designated SEQ ID:45661, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67330] Another function of VGAM1958 is therefore inhibition of LOC255057 (Accession XM\_170903). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255057. LOC255082 (Accession XM\_172843) is another VGAM1958 host target gene. LOC255082 BINDING SITE1 and LOC255082 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC255082, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255082 BINDING SITE1 and LOC255082 BINDING SITE2, designated SEQ ID:46118 and SEQ ID:46120 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67331] Another function of VGAM1958 is therefore inhibition of LOC255082 (Accession XM\_172843). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC255082. LOC255645 (Accession XM\_172967) is another VGAM1958 host target gene. LOC255645 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255645, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255645 BINDING SITE, designated SEQ ID:46222, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67332] Another function of VGAM1958 is therefore inhibition of LOC255645 (Accession XM\_172967). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255645. LOC255995 (Accession XM\_173071) is another VGAM1958 host target gene. LOC255995 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255995, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255995 BINDING SITE, designated SEQ ID:46324, to the nucleotide sequence of VGAM1958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4669.

[67333] Another function of VGAM1958 is therefore inhibition of LOC255995 (Accession XM\_173071). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255995. LOC256158 (Accession XM\_175125) is another VGAM1958 host target gene. LOC256158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE, designated SEQ ID:46636, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67334] Another function of VGAM1958 is therefore inhibition of LOC256158 (Accession XM\_175125). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256158. LOC256790 (Accession XM\_170679) is another VGAM1958 host target gene. LOC256790 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256790, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256790 BINDING SITE, designated SEQ ID:45460, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67335] Another function of VGAM1958 is therefore inhibition of LOC256790 (Accession XM\_170679). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256790. LOC256848 (Accession XM\_174050) is another VGAM1958 host target gene. LOC256848 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256848 BINDING SITE, designated SEQ ID:46570, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67336] Another function of VGAM1958 is therefore inhibition of LOC256848 (Accession XM\_174050). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC256848. LOC257054 (Accession XM\_171010) is another VGAM1958 host target gene. LOC257054 BINDING SITE1 and LOC257054 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC257054, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257054 BINDING SITE1 and LOC257054 BINDING SITE2, designated SEQ ID:45779 and SEQ ID:45784 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67337] Another function of VGAM1958 is therefore inhibition of LOC257054 (Accession XM\_171010). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257054. LOC257354 (Accession XM\_170810) is another VGAM1958 host target gene. LOC257354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC257354 BINDING SITE, designated SEQ ID:45575, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67338] Another function of VGAM1958 is therefore inhibition of LOC257354 (Accession XM\_170810). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257354. LOC257451 (Accession XM\_170960) is another VGAM1958 host target gene. LOC257451 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257451 BINDING SITE, designated SEQ ID:45743, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67339] Another function of VGAM1958 is therefore inhibition of LOC257451 (Accession XM\_170960). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257451. LOC257463 (Accession XM\_048605) is an-

other VGAM1958 host target gene. LOC257463 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257463 BINDING SITE, designated SEQ ID:35210, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67340] Another function of VGAM1958 is therefore inhibition of LOC257463 (Accession XM\_048605). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257463. LOC257472 (Accession XM\_170812) is another VGAM1958 host target gene. LOC257472 BINDING SITE1 and LOC257472 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC257472, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257472 BINDING SITE1 and LOC257472 BINDING SITE2, designated SEQ ID:45593 and SEQ ID:45594 respectively, to the nucleotide se-

quence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67341] Another function of VGAM1958 is therefore inhibition of LOC257472 (Accession XM\_170812). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257472. LOC51219 (Accession NM\_016418) is another VGAM1958 host target gene. LOC51219 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51219 BINDING SITE, designated SEQ ID:18545, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67342] Another function of VGAM1958 is therefore inhibition of LOC51219 (Accession NM\_016418). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51219. LOC51236 (Accession NM\_016458) is another VGAM1958 host target gene. LOC51236 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC51236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51236 BINDING SITE, designated SEQ ID:18571, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67343] Another function of VGAM1958 is therefore inhibition of LOC51236 (Accession NM\_016458). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51236. LOC51279 (Accession NM\_016546) is another VGAM1958 host target gene. LOC51279 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51279, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51279 BINDING SITE, designated SEQ ID:18618, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67344] Another function of VGAM1958 is therefore inhibition of LOC51279 (Accession NM\_016546). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51279. LOC51644 (Accession NM\_016057) is another VGAM1958 host target gene. LOC51644 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51644 BINDING SITE, designated SEQ ID:18129, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67345] Another function of VGAM1958 is therefore inhibition of LOC51644 (Accession NM\_016057). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51644. LOC54499 (Accession XM\_047479) is another VGAM1958 host target gene. LOC54499 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC54499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC54499 BINDING SITE, designated SEQ ID:34965, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67346] Another function of VGAM1958 is therefore inhibition of LOC54499 (Accession XM\_047479). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC54499. LOC55580 (Accession NM\_017571) is another VGAM1958 host target gene. LOC55580 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC55580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC55580 BINDING SITE, designated SEQ ID:18994, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67347] Another function of VGAM1958 is therefore inhibition of LOC55580 (Accession NM\_017571). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC55580. LOC56181 (Accession XM\_170954) is another VGAM1958 host target gene. LOC56181 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56181 BINDING SITE, designated SEQ ID:45739, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67348] Another function of VGAM1958 is therefore inhibition of LOC56181 (Accession XM\_170954). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56181. LOC56270 (Accession NM\_019613) is another VGAM1958 host target gene. LOC56270 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC56270, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56270 BINDING SITE, designated SEQ ID:21231, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67349] Another function of VGAM1958 is therefore inhibition of



LOC56270 (Accession NM\_019613). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56270. LOC56899 (Accession NM\_020140) is another VGAM1958 host target gene. LOC56899 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56899, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56899 BINDING SITE, designated SEQ ID:21336, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67350] Another function of VGAM1958 is therefore inhibition of LOC56899 (Accession NM\_020140). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56899. LOC57826 (Accession NM\_021183) is another VGAM1958 host target gene. LOC57826 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC57826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC57826 BINDING SITE, designated SEQ ID:22158, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67351] Another function of VGAM1958 is therefore inhibition of LOC57826 (Accession NM\_021183). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57826. LOC64744 (Accession XM\_029830) is another VGAM1958 host target gene. LOC64744 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC64744, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC64744 BINDING SITE, designated SEQ ID:30952, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67352] Another function of VGAM1958 is therefore inhibition of LOC64744 (Accession XM\_029830). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC64744. LOC90038 (Accession XM\_028305) is another

VGAM1958 host target gene. LOC90038 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90038 BINDING SITE, designated SEQ ID:30647, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67353] Another function of VGAM1958 is therefore inhibition of LOC90038 (Accession XM\_028305). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90038. LOC90092 (Accession XM\_028862) is another VGAM1958 host target gene. LOC90092 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90092 BINDING SITE, designated SEQ ID:30781, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67354] Another function of VGAM1958 is therefore inhibition of LOC90092 (Accession XM\_028862). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90092. LOC90133 (Accession XM\_029323) is another VGAM1958 host target gene. LOC90133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90133 BINDING SITE, designated SEQ ID:30868, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67355] Another function of VGAM1958 is therefore inhibition of LOC90133 (Accession XM\_029323). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90133. LOC90148 (Accession XM\_029430) is another VGAM1958 host target gene. LOC90148 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90148, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90148 BINDING SITE, designated SEQ ID:30891, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67356] Another function of VGAM1958 is therefore inhibition of LOC90148 (Accession XM\_029430). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90148. LOC90170 (Accession XM\_029589) is another VGAM1958 host target gene. LOC90170 BINDING SITE1 and LOC90170 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC90170, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90170 BINDING SITE1 and LOC90170 BINDING SITE2, designated SEQ ID:30912 and SEQ ID:30914 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67357] Another function of VGAM1958 is therefore inhibition of LOC90170 (Accession XM\_029589). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90170. LOC90233 (Accession NM\_138347) is another VGAM1958 host target gene. LOC90233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90233 BINDING SITE, designated SEQ ID:28743, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67358] Another function of VGAM1958 is therefore inhibition of LOC90233 (Accession NM\_138347). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90233. LOC90249 (Accession XM\_030300) is another VGAM1958 host target gene. LOC90249 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC90249 BINDING SITE, designated SEQ ID:31012, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67359] Another function of VGAM1958 is therefore inhibition of LOC90249 (Accession XM\_030300). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90249. LOC90288 (Accession XM\_030669) is another VGAM1958 host target gene. LOC90288 BINDING SITE1 and LOC90288 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC90288, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90288 BINDING SITE1 and LOC90288 BINDING SITE2, designated SEQ ID:31109 and SEQ ID:31110 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67360] Another function of VGAM1958 is therefore inhibition of LOC90288 (Accession XM\_030669). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90288. LOC90485 (Accession XM\_032059) is another VGAM1958 host target gene. LOC90485 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90485, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90485 BINDING SITE, designated SEQ ID:31554, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67361] Another function of VGAM1958 is therefore inhibition of LOC90485 (Accession XM\_032059). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90485. LOC90632 (Accession XM\_033067) is another VGAM1958 host target gene. LOC90632 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90632, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90632 BINDING SITE, designated SEQ ID:31829, to the nucleotide sequence of VGAM1958 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4669.

[67362] Another function of VGAM1958 is therefore inhibition of LOC90632 (Accession XM\_033067). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90632. LOC90777 (Accession XM\_034052) is another VGAM1958 host target gene. LOC90777 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90777, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90777 BINDING SITE, designated SEQ ID:31993, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67363] Another function of VGAM1958 is therefore inhibition of LOC90777 (Accession XM\_034052). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90777. LOC90784 (Accession XM\_034109) is another VGAM1958 host target gene. LOC90784 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90784, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90784 BINDING SITE, designated SEQ ID:32002, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67364] Another function of VGAM1958 is therefore inhibition of LOC90784 (Accession XM\_034109). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90784. LOC90786 (Accession XM\_034127) is another VGAM1958 host target gene. LOC90786 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90786 BINDING SITE, designated SEQ ID:32011, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67365] Another function of VGAM1958 is therefore inhibition of LOC90786 (Accession XM\_034127). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC90786. LOC90826 (Accession XM\_034321) is another VGAM1958 host target gene. LOC90826 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90826 BINDING SITE, designated SEQ ID:32053, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67366] Another function of VGAM1958 is therefore inhibition of LOC90826 (Accession XM\_034321). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90826. LOC90906 (Accession XM\_034809) is another VGAM1958 host target gene. LOC90906 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90906 BINDING SITE, designated SEQ ID:32147, to the

nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67367] Another function of VGAM1958 is therefore inhibition of LOC90906 (Accession XM\_034809). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90906. LOC91050 (Accession XM\_035703) is another VGAM1958 host target gene. LOC91050 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91050, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91050 BINDING SITE, designated SEQ ID:32333, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67368] Another function of VGAM1958 is therefore inhibition of LOC91050 (Accession XM\_035703). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91050. LOC91097 (Accession XM\_035977) is another VGAM1958 host target gene. LOC91097 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC91097, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91097 BINDING SITE, designated SEQ ID:32369, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67369] Another function of VGAM1958 is therefore inhibition of LOC91097 (Accession XM\_035977). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91097. LOC91149 (Accession XM\_036480) is another VGAM1958 host target gene. LOC91149 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91149, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91149 BINDING SITE, designated SEQ ID:32453, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67370] Another function of VGAM1958 is therefore inhibition of LOC91149 (Accession XM\_036480). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91149. LOC91301 (Accession XM\_037564) is another VGAM1958 host target gene. LOC91301 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91301 BINDING SITE, designated SEQ ID:32650, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67371] Another function of VGAM1958 is therefore inhibition of LOC91301 (Accession XM\_037564). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91301. LOC91355 (Accession XM\_037825) is another VGAM1958 host target gene. LOC91355 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91355, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC91355 BINDING SITE, designated SEQ ID:32701, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67372] Another function of VGAM1958 is therefore inhibition of LOC91355 (Accession XM\_037825). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91355. LOC91445 (Accession XM\_018516) is another VGAM1958 host target gene. LOC91445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91445 BINDING SITE, designated SEQ ID:30365, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67373] Another function of VGAM1958 is therefore inhibition of LOC91445 (Accession XM\_018516). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91445. LOC91531 (Accession XM\_038998) is another VGAM1958 host target gene. LOC91531 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91531, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91531 BINDING SITE, designated SEQ ID:32972, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67374] Another function of VGAM1958 is therefore inhibition of LOC91531 (Accession XM\_038998). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91531. LOC91632 (Accession XM\_039721) is another VGAM1958 host target gene. LOC91632 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91632, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91632 BINDING SITE, designated SEQ ID:33164, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67375] Another function of VGAM1958 is therefore inhibition of



LOC91632 (Accession XM\_039721). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91632. LOC91759 (Accession XM\_040467) is another VGAM1958 host target gene. LOC91759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91759 BINDING SITE, designated SEQ ID:33300, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67376] Another function of VGAM1958 is therefore inhibition of LOC91759 (Accession XM\_040467). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91759. LOC91812 (Accession XM\_040857) is another VGAM1958 host target gene. LOC91812 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC91812 BINDING SITE, designated SEQ ID:33391, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67377] Another function of VGAM1958 is therefore inhibition of LOC91812 (Accession XM\_040857). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91812. LOC91813 (Accession XM\_040862) is another VGAM1958 host target gene. LOC91813 BINDING SITE1 and LOC91813 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC91813, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91813 BINDING SITE1 and LOC91813 BINDING SITE2, designated SEQ ID:33394 and SEQ ID:33399 respectively, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67378] Another function of VGAM1958 is therefore inhibition of LOC91813 (Accession XM\_040862). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC91813. LOC92249 (Accession XM\_043814) is another VGAM1958 host target gene. LOC92249 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC92249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92249 BINDING SITE, designated SEQ ID:34018, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67379] Another function of VGAM1958 is therefore inhibition of LOC92249 (Accession XM\_043814). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92249. LOC92360 (Accession XM\_044589) is another VGAM1958 host target gene. LOC92360 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC92360, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92360 BINDING SITE, designated SEQ ID:34240, to the

nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67380] Another function of VGAM1958 is therefore inhibition of LOC92360 (Accession XM\_044589). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92360. LOC92492 (Accession XM\_045396) is another VGAM1958 host target gene. LOC92492 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92492, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92492 BINDING SITE, designated SEQ ID:34453, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67381] Another function of VGAM1958 is therefore inhibition of LOC92492 (Accession XM\_045396). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92492. LOC92499 (Accession XM\_045450) is another VGAM1958 host target gene. LOC92499 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC92499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92499 BINDING SITE, designated SEQ ID:34462, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67382] Another function of VGAM1958 is therefore inhibition of LOC92499 (Accession XM\_045450). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92499. LOC92973 (Accession XM\_048529) is another VGAM1958 host target gene. LOC92973 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC92973, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92973 BINDING SITE, designated SEQ ID:35186, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67383] Another function of VGAM1958 is therefore inhibition of LOC92973 (Accession XM\_048529). Accordingly, utilities

of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92973. LOC93017 (Accession XM\_048772) is another VGAM1958 host target gene. LOC93017 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93017 BINDING SITE, designated SEQ ID:35252, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67384] Another function of VGAM1958 is therefore inhibition of LOC93017 (Accession XM\_048772). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93017. LOC93052 (Accession XM\_048905) is another VGAM1958 host target gene. LOC93052 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC93052 BINDING SITE, designated SEQ ID:35303, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67385] Another function of VGAM1958 is therefore inhibition of LOC93052 (Accession XM\_048905). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93052. LOC93613 (Accession XM\_052568) is another VGAM1958 host target gene. LOC93613 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93613, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93613 BINDING SITE, designated SEQ ID:35996, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67386] Another function of VGAM1958 is therefore inhibition of LOC93613 (Accession XM\_052568). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93613. LOC96597 (Accession XM\_039922) is another VGAM1958 host target gene. LOC96597 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC96597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC96597 BINDING SITE, designated SEQ ID:33226, to the nucleotide sequence of VGAM1958 RNA, herein designated VGAM RNA, also designated SEQ ID:4669.

[67387] Another function of VGAM1958 is therefore inhibition of LOC96597 (Accession XM\_039922). Accordingly, utilities of VGAM1958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC96597. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1959 (VGAM1959) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[67388] VGAM1959 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1959 was detected is described hereinabove with reference to Figs. 1-8.



[67389] VGAM1959 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1959 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[67390] VGAM1959 gene encodes a VGAM1959 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1959 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1959 precursor RNA is designated SEQ ID:1945, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1945 is located at position 16300 relative to the genome of Macaca Mulatta Rhadinovirus.

[67391] VGAM1959 precursor RNA folds onto itself, forming VGAM1959 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[67392] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1959 folded precursor RNA into VGAM1959 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1959 RNA is designated SEQ ID:4670, and is provided hereinbelow with reference to the sequence listing part.

[67393] VGAM1959 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1959 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1959 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[67394] VGAM1959 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1959 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1959 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1959 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1959 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[67395] The complementary binding of VGAM1959 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1959 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1959 host target RNA into VGAM1959 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[67396] It is appreciated that VGAM1959 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1959 host target genes. The mRNA of each one of this plurality of VGAM1959 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1959 RNA, herein designated VGAM RNA, and which when bound by VGAM1959 RNA causes inhibition of translation of respective one or more VGAM1959 host target proteins.

[67397] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1959 gene, herein designated VGAM GENE, on one or more VGAM1959 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[67398] It is yet further appreciated that a function of VGAM1959 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1959 correlate with, and may be deduced from, the identity of the host target genes which VGAM1959 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[67399] Nucleotide sequences of the VGAM1959 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1959 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1959 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1959 are further described hereinbelow with reference to Table 1.

[67400] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1959 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1959 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[67401] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1959 gene, herein designated VGAM is inhibition of expression of VGAM1959 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1959 correlate with, and may be deduced from, the identity of the target genes which VGAM1959 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[67402] Amiloride-sensitive Cation Channel 2, Neuronal (ACCN2, Accession NM\_020039) is a VGAM1959 host target gene. ACCN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACCN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of ACCN2 BINDING SITE, designated SEQ ID:21298, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67403] A function of VGAM1959 is therefore inhibition of Amiloride-sensitive Cation Channel 2, Neuronal (ACCN2, Accession NM\_020039). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACCN2. ACK1 (Accession NM\_005781) is another VGAM1959 host target gene. ACK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACK1 BINDING SITE, designated SEQ ID:12359, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67404] Another function of VGAM1959 is therefore inhibition of ACK1 (Accession NM\_005781). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ACK1. A Disintegrin and Metalloproteinase Domain 19 (meltrin beta) (ADAM19, Accession NM\_033274) is another VGAM1959 host target gene. ADAM19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAM19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM19 BINDING SITE, designated SEQ ID:27096, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67405] Another function of VGAM1959 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 19 (meltrin beta) (ADAM19, Accession NM\_033274), a gene which participates in the proteolytic processing of beta-type neuregulin isoforms. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM19. The function of ADAM19 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. A Disintegrin-like and Metalloprotease



(reprolysin type) with Thrombospondin Type 1 Motif, 13 (ADAMTS13, Accession NM\_139028) is another VGAM1959 host target gene. ADAMTS13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAMTS13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS13 BINDING SITE, designated SEQ ID:29129, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67406] Another function of VGAM1959 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 13 (ADAMTS13, Accession NM\_139028), a gene which cleaves aggrecan, a cartilage proteoglycan, and may be involved in its turnover. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS13. The function of ADAMTS13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM131. Adenylate Cyclase 6 (ADCY6, Accession

NM\_020983) is another VGAM1959 host target gene. ADCY6 BINDING SITE1 and ADCY6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADCY6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY6 BINDING SITE1 and ADCY6 BINDING SITE2, designated SEQ ID:21978 and SEQ ID:17591 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67407] Another function of VGAM1959 is therefore inhibition of Adenylate Cyclase 6 (ADCY6, Accession NM\_020983), a gene which this a membrane-bound,  $Ca^{2+}$ -inhibitable adenylyl cyclase (by similarity). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY6. The function of ADCY6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM22. Adducin 2 (beta) (ADD2, Accession NM\_017483) is another VGAM1959 host target gene. ADD2 BINDING SITE1 through ADD2 BINDING SITE7 are

HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADD2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADD2 BINDING SITE1 through ADD2 BINDING SITE7, designated SEQ ID:18936, SEQ ID:18939, SEQ ID:18941, SEQ ID:18944, SEQ ID:18947, SEQ ID:18949 and SEQ ID:6793 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67408] Another function of VGAM1959 is therefore inhibition of Adducin 2 (beta) (ADD2, Accession NM\_017483), a gene which membrane-cytoskeleton- protein that promotes the assembly of the spectrin-actin network. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADD2. The function of ADD2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1185.1-acylglycerol-3-phosphate O-acyltransferase 2 (lysophosphatidic acid acyltransferase, beta) (AGPAT2, Accession XM\_038030) is another VGAM1959 host target gene. AGPAT2 BINDING SITE1 and

AGPAT2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AGPAT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGPAT2 BINDING SITE1 and AGPAT2 BINDING SITE2, designated SEQ ID:32746 and SEQ ID:13119 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67409] Another function of VGAM1959 is therefore inhibition of 1-acylglycerol-3-phosphate O-acyltransferase 2 (lysophosphatidic acid acyltransferase, beta) (AGPAT2, Accession XM\_038030). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGPAT2. A Kinase (PRKA) Anchor Protein 1 (AKAP1, Accession NM\_003488) is another VGAM1959 host target gene. AKAP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AKAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

AKAP1 BINDING SITE, designated SEQ ID:9580, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67410] Another function of VGAM1959 is therefore inhibition of A Kinase (PRKA) Anchor Protein 1 (AKAP1, Accession NM\_003488), a gene which binds to type i and ii regulatory subunits of protein kinase a . Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP1. The function of AKAP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1392. Anaplastic Lymphoma Kinase (Ki-1) (ALK, Accession XM\_055726) is another VGAM1959 host target gene. ALK BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ALK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALK BINDING SITE, designated SEQ ID:36320, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67411] Another function of VGAM1959 is therefore inhibition of

Anaplastic Lymphoma Kinase (Ki-1) (ALK, Accession XM\_055726). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALK. Autocrine Motility Factor Receptor (AMFR, Accession NM\_138958) is another VGAM1959 host target gene. AMFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMFR BINDING SITE, designated SEQ ID:29065, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67412] Another function of VGAM1959 is therefore inhibition of Autocrine Motility Factor Receptor (AMFR, Accession NM\_138958), a gene which acts to stimulate migration of fibrosarcoma cells. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMFR. The function of AMFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM440. Ankyrin 1, Erythrocytic (ANK1, Accession NM\_020476) is another VGAM1959 host target gene. ANK1 BINDING SITE1 through ANK1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ANK1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK1 BINDING SITE1 through ANK1 BINDING SITE3, designated SEQ ID:21731, SEQ ID:30282 and SEQ ID:5478 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67413] Another function of VGAM1959 is therefore inhibition of Ankyrin 1, Erythrocytic (ANK1, Accession NM\_020476). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK1. Apolipoprotein L, 1 (APOL1, Accession NM\_003661) is another VGAM1959 host target gene. APOL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of APOL1 BINDING SITE, designated SEQ ID:9734, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67414] Another function of VGAM1959 is therefore inhibition of Apolipoprotein L, 1 (APOL1, Accession NM\_003661), a gene which may participate in reverse cholesterol transport from peripheral cells to the liver. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL1. The function of APOL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM235. Rho GTPase Activating Protein 6 (ARHGAP6, Accession NM\_001174) is another VGAM1959 host target gene. ARHGAP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGAP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP6 BINDING SITE, designated SEQ ID:6849, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also des-



ignated SEQ ID:4670.

[67415] Another function of VGAM1959 is therefore inhibition of Rho GTPase Activating Protein 6 (ARHGAP6, Accession NM\_001174), a gene which activates the rho-type GTPases by converting them to an inactive GTP-bound state. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP6. The function of ARHGAP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.ATPase, Na<sup>+</sup>/K<sup>+</sup> Transporting, Beta 2 Polypeptide (ATP1B2, Accession NM\_001678) is another VGAM1959 host target gene. ATP1B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP1B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1B2 BINDING SITE, designated SEQ ID:7395, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67416] Another function of VGAM1959 is therefore inhibition of

ATPase, Na<sup>+</sup>/K<sup>+</sup> Transporting, Beta 2 Polypeptide (ATP1B2, Accession NM\_001678), a gene which catalyzes the hydrolysis of ATP coupled with the exchange of Na<sup>+</sup>/K<sup>+</sup> ions across the plasma membrane. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1B2. The function of ATP1B2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. ATPase, Ca<sup>++</sup> Transporting, Ubiquitous (ATP2A3, Accession NM\_005173) is another VGAM1959 host target gene. ATP2A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP2A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP2A3 BINDING SITE, designated SEQ ID:11674, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67417] Another function of VGAM1959 is therefore inhibition of ATPase, Ca<sup>++</sup> Transporting, Ubiquitous (ATP2A3, Accession NM\_005173). Accordingly, utilities of VGAM1959 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP2A3. ATPase, Cu<sup>++</sup> Transporting, Beta Polypeptide (Wilson disease) (ATP7B, Accession NM\_000053) is another VGAM1959 host target gene. ATP7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP7B BINDING SITE, designated SEQ ID:5510, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67418] Another function of VGAM1959 is therefore inhibition of ATPase, Cu<sup>++</sup> Transporting, Beta Polypeptide (Wilson disease) (ATP7B, Accession NM\_000053). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP7B. ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM\_036933) is another VGAM1959 host target gene. ATP8B2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ATP8B2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8B2 BINDING SITE, designated SEQ ID:32512, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67419] Another function of VGAM1959 is therefore inhibition of ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM\_036933). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8B2. B-cell CLL/lymphoma 6 (zinc finger protein 51) (BCL6, Accession NM\_001706) is another VGAM1959 host target gene. BCL6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BCL6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL6 BINDING SITE, designated SEQ ID:7429, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67420] Another function of VGAM1959 is therefore inhibition of B-cell CLL/lymphoma 6 (zinc finger protein 51) (BCL6, Ac-

cession NM\_001706), a gene which is involved in the generation and maintenance of both T and B cells during immune responses. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL6. The function of BCL6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM481. B-cell CLL/lymphoma 7A (BCL7A, Accession NM\_020993) is another VGAM1959 host target gene. BCL7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL7A BINDING SITE, designated SEQ ID:21992, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67421] Another function of VGAM1959 is therefore inhibition of B-cell CLL/lymphoma 7A (BCL7A, Accession NM\_020993). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL7A. BCRP2 (Accession

XM\_031102) is another VGAM1959 host target gene.

BCRP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BCRP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCRP2 BINDING SITE, designated SEQ ID:31273, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67422] Another function of VGAM1959 is therefore inhibition of BCRP2 (Accession XM\_031102). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCRP2. BLAME (Accession NM\_020125) is another VGAM1959 host target gene. BLAME BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BLAME, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLAME BINDING SITE, designated SEQ ID:21308, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4670.

[67423] Another function of VGAM1959 is therefore inhibition of BLAME (Accession NM\_020125). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLAME. Basonuclin (BNC, Accession NM\_001717) is another VGAM1959 host target gene. BNC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BNC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BNC BINDING SITE, designated SEQ ID:7451, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67424] Another function of VGAM1959 is therefore inhibition of Basonuclin (BNC, Accession NM\_001717), a gene which plays a role in the maintenance of proliferative capacity and prevention of terminal differentiation of keratinocytes. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BNC. The function of BNC and its association with various diseases and clinical condi-

tions, has been established by previous studies, as described hereinabove with reference to VGAM1514.BTG Family, Member 2 (BTG2, Accession NM\_006763) is another VGAM1959 host target gene. BTG2 BINDING SITE1 and BTG2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BTG2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTG2 BINDING SITE1 and BTG2 BINDING SITE2, designated SEQ ID:13623 and SEQ ID:13624 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67425] Another function of VGAM1959 is therefore inhibition of BTG Family, Member 2 (BTG2, Accession NM\_006763). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTG2. Caspase 10, Apoptosis-related Cysteine Protease (CASP10, Accession NM\_032976) is another VGAM1959 host target gene. CASP10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CASP10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP10 BINDING SITE, designated SEQ ID:26834, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67426] Another function of VGAM1959 is therefore inhibition of Caspase 10, Apoptosis-related Cysteine Protease (CASP10, Accession NM\_032976), a gene which is one aspartate-specific cysteine protease and important in death receptor signaling or other cellular processes. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP10. The function of CASP10 has been established by previous studies. Wang et al. (2001) showed that caspase-10 can function independently of caspase-8 in initiating FAS- and tumor necrosis factor-related apoptosis-inducing ligand-receptor-mediated apoptosis. Moreover, FAS crosslinking in primary human T cells leads to the recruitment and activation of caspase-10. They showed that the death-effector domains of caspases 8 and 10 interact with the death-effector domain of FADD. Nonetheless, they found that caspases 8 and 10 may have different apoptosis substrates and therefore potentially

distinct roles in death receptor signaling or other cellular processes. By a candidate gene mutation search strategy, Wang et al. (1999) identified independent missense mutations in the CASP10 gene in 2 kindreds with type II autoimmune lymphoproliferative syndrome (ALPS2; 603909) characterized by abnormal lymphocyte and dendritic cell homeostasis and immune regulatory defects. The mutations (601762.0001 and 601762.0002) resulted in amino acid substitutions that decreased caspase activity and interfered with death receptor-induced apoptosis, particularly that stimulated by Fas ligand (OMIM Ref. No. 134638) and TRAIL (OMIM Ref. No. 603598). These results provided evidence that inherited nonlethal caspase abnormalities cause pleiotropic apoptosis defects underlying autoimmunity in ALPS2. To explore the possibility that mutation in the CASP10 gene might be involved in the development of non-Hodgkin lymphoma (NHL; 605027), Shin et al. (2002) analyzed the entire coding region and all splice sites of the CASP10 gene for the detection of somatic mutations in 117 human NHLs. Seventeen NHLs (14.5%) had CASP10 mutations, of which 3 were identified in the coding regions of the prodomain, 11 in the p17 large protease subunit, and 3 in the p12 small protease

subunit. There were 2 frameshift mutations and 1 non-sense mutation; the remaining 14 were missense mutations. Shin et al. (2002) expressed the tumor-derived CASP10 mutants in 293 cells and found that apoptosis was suppressed. These data suggested that the inactivating mutations of the CASP10 gene may lead to the loss of its apoptotic function and contribute to the pathogenesis of some human NHLs.

[67427] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67428] Wang, J.; Chun, H. J.; Wong, W.; Spencer, D. M.; Lenardo, M. J. : Caspase-10 is an initiator caspase in death receptor signaling. *Proc. Nat. Acad. Sci.* 98: 13884-13888, 2001. ; and

[67429] Wang, J.; Zheng, L.; Lobito, A.; Chan, F. K.; Dale, J.; Sneller, M.; Yao, X.; Puck, J. M.; Straus, S. E.; Lenardo, M. J. : Inherited human caspase 10 mutations underlie defective lympho.

[67430] Further studies establishing the function and utilities of CASP10 are found in John Hopkins OMIM database record ID 601762, and in cited publications numbered 7119-6717 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Cyclin F (CCNF, Accession NM\_001761) is another VGAM1959 host target gene. CCNF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCNF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNF BINDING SITE, designated SEQ ID:7526, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67431] Another function of VGAM1959 is therefore inhibition of Cyclin F (CCNF, Accession NM\_001761), a gene which likely to be involved in the control of the cell cycle during S phase and G2. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNF. The function of CCNF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM367. Cadherin 5, Type 2, VE-cadherin (vascular epithelium) (CDH5, Accession NM\_001795) is another VGAM1959 host target gene. CDH5 BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by CDH5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH5 BINDING SITE, designated SEQ ID:7549, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67432] Another function of VGAM1959 is therefore inhibition of Cadherin 5, Type 2, VE-cadherin (vascular epithelium) (CDH5, Accession NM\_001795), a gene which associates with alpha-catenin forming a link to the cytoskeleton. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH5. The function of CDH5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1342. Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM\_052988) is another VGAM1959 host target gene. CDK10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDK10, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK10 BINDING SITE, designated SEQ ID:27556, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67433] Another function of VGAM1959 is therefore inhibition of Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM\_052988), a gene which plays a pivotal role in the regulation of the eukaryotic cell cycle. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK10. The function of CDK10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM193. Cerebellar Degeneration-related Protein 2, 62kDa (CDR2, Accession XM\_071866) is another VGAM1959 host target gene. CDR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDR2 BINDING SITE, designated SEQ ID:37428, to the nucleotide se-

quence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67434] Another function of VGAM1959 is therefore inhibition of Cerebellar Degeneration-related Protein 2, 62kDa (CDR2, Accession XM\_071866), a gene which plays a role in cytokinesis, cell shape, and functions such as secretion and capping. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDR2. The function of CDR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128. Carcinoembryonic Antigen-related Cell Adhesion Molecule 1 (biliary glycoprotein) (CEACAM1, Accession NM\_001712) is another VGAM1959 host target gene. CEACAM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CEACAM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEACAM1 BINDING SITE, designated SEQ ID:7441, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ

ID:4670.

[67435] Another function of VGAM1959 is therefore inhibition of Carcinoembryonic Antigen-related Cell Adhesion Molecule 1 (biliary glycoprotein) (CEACAM1, Accession NM\_001712), a gene which is a major effector of VEGF and may be a target for the inhibition of tumor angiogenesis. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEACAM1. The function of CEACAM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM93.Cadherin, EGF LAG Seven-pass G-type Receptor 3 (flamingo homolog, Drosophila) (CELSR3, Accession NM\_001407) is another VGAM1959 host target gene. CELSR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CELSR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CELSR3 BINDING SITE, designated SEQ ID:7103, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ



ID:4670.

[67436] Another function of VGAM1959 is therefore inhibition of Cadherin, EGF LAG Seven-pass G-type Receptor 3 (flamingo homolog, Drosophila) (CELSR3, Accession NM\_001407), a gene which interacts in a homophilic manner in connecting cells. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CELSR3. The function of CELSR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM893. Centrosomal Protein 2 (CEP2, Accession NM\_007186) is another VGAM1959 host target gene. CEP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CEP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP2 BINDING SITE, designated SEQ ID:14043, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67437] Another function of VGAM1959 is therefore inhibition of Centrosomal Protein 2 (CEP2, Accession NM\_007186), a

gene which interacts with TC10 and CDC42. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEP2. The function of CEP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM329. Chorionic Gonadotropin, Beta Polypeptide (CGB, Accession NM\_000737) is another VGAM1959 host target gene. CGB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CGB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGB BINDING SITE, designated SEQ ID:6394, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67438] Another function of VGAM1959 is therefore inhibition of Chorionic Gonadotropin, Beta Polypeptide (CGB, Accession NM\_000737), a gene which stimulates the ovaries to synthesize the steroids. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGB. The function

of CGB has been established by previous studies. Human chorionic gonadotropin (hCG) is a glycoprotein hormone produced by trophoblastic cells of the placenta beginning 10 to 12 days after conception. Maintenance of the fetus in the first trimester of pregnancy requires the production of hCG, which binds to the corpus luteum of the ovary which is stimulated to produce progesterone which in turn maintains the secretory endometrium. See 118850.

Boorstein et al. (1982) concluded that the beta subunit of CG is encoded by at least 8 genes arranged in tandem and inverted pairs. They stated that 'until sequence analysis is complete, we cannot exclude the possibility that the eight genes include some pseudogenes or the related gene, beta-LH.' The beta subunits of luteinizing hormone (LHB) and CG show about 82% amino acid homology. The homology with beta-FSH and beta-TSH is much lower. Policastro et al. (1983, 1986) found 6 nonallelic copies of the CGB gene and a single-copy LHB gene. All were contained in a single 58-kb EcoRI fragment. The hCG beta-subunit is unique in the family of beta-containing glycoprotein hormones in that it contains an extension of 29 amino acids at its COOH end. Amato et al. (2002) reported a patient with a 9-year history of secondary infertility due to

an anti-CG autoantibody. Although she had regular menstrual cycles, had conceived spontaneously, and had good hormonal and follicular responses to gonadotropic stimulation regimens during the in vitro fertilization workup, she presented with apparent recurrent pregnancy loss associated with prolonged raised CG levels. She was found to have specific, low-affinity, but high-capacity anti-CG antibody. Crossreaction with recombinant FSH, recombinant LH, CG-alpha, and CG-beta was low. In addition, heat-inactivated serum and the affinity-purified IgG were shown to inhibit the action of CG in an in vitro bioassay. The authors concluded that the persisting titer of the antibody was responsible for the patient's infertility.

[67439] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67440] Policastro, P. F.; Daniels-McQueen, S.; Carle, G.; Boime, I. : A map of the hCG-beta-LH-beta gene cluster. J. Biol. Chem. 261: 5907-5916, 1986. ; and

[67441] Amato, F.; Warnes, G. M.; Kirby, C. A.; Norman, R. J. : Infertility caused by hCG autoantibody. J. Clin. Endocr. Metab. 87: 993-997, 2002.

[67442] Further studies establishing the function and utilities of

CGB are found in John Hopkins OMIM database record ID 118860, and in cited publications numbered 12221, 12289–12294, 10886, 1222 and 12295–12298 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CGTHBA (Accession NM\_012075) is another VGAM1959 host target gene. CGTHBA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CGTHBA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGTHBA BINDING SITE, designated SEQ ID:14356, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67443] Another function of VGAM1959 is therefore inhibition of CGTHBA (Accession NM\_012075). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGTHBA. Chromodomain Helicase DNA Binding Protein 2 (CHD2, Accession NM\_001271) is another VGAM1959 host target gene. CHD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded

by CHD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHD2 BINDING SITE, designated SEQ ID:6938, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67444] Another function of VGAM1959 is therefore inhibition of Chromodomain Helicase DNA Binding Protein 2 (CHD2, Accession NM\_001271). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHD2. Cholinergic Receptor, Nicotinic, Epsilon Polypeptide (CHRNE, Accession NM\_000080) is another VGAM1959 host target gene. CHRNE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRNE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRNE BINDING SITE, designated SEQ ID:5522, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67445] Another function of VGAM1959 is therefore inhibition of Cholinergic Receptor, Nicotinic, Epsilon Polypeptide (CHRNE, Accession NM\_000080), a gene which leads to opening of an ion-conducting channel across the plasma membrane. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRNE. The function of CHRNE has been established by previous studies. Witzemann et al. (1996) noted that in mammalian muscle the functional properties of end-plate channels change during postnatal development. The length of channel-opening bursts decreases and, as a consequence, the duration of miniature end-plate current (mEPC) decreases, whereas the conductance and the  $\text{Ca}^{2+}$  permeability of end-plate channels increase. The underlying molecular mechanism is a switch in the expression of acetylcholine receptor subunit genes shortly after birth. The gamma-subunit (CHRNA7) is repressed while the epsilon-subunit gene is activated selectively in the myonuclei underlying the synapse. To investigate the significance of the CHRNA7/CHRNE switch for motor behavior, Witzemann et al. (1996) ablated the Chrne gene in mouse embryonic stem (es) cells by homologous recombination and injected correctly engineered cells of 2

independently isolated clones into C57BL/6 blastocysts. Chimeric male mice derived from both clones showed germline transmission of the targeted allele. Homozygous mutant animals showed that after apparently normal development in early neonatal life, neuromuscular transmission was progressively impaired. The lack of epsilon subunits caused muscle weakness, defects in motor behavior, and premature death 2 to 3 months after birth. Their results demonstrated that postnatal incorporation of epsilon subunits in acetylcholine receptors into the end plate is essential for normal development of skeletal muscle.

Ohno et al. (1997) found that each of 3 unrelated patients with the congenital myasthenic syndrome (OMIM Ref. No. 601462) were compound heterozygotes (heteroallelic) for a nonsense mutation and a missense mutation. Each nonsense mutation predicted truncation of the epsilon subunit in its extracellular domain, and expression studies in human embryonic kidney fibroblasts (HEK cells) indicated that they were null mutations. Each missense mutation significantly reduced acetylcholine receptor expression; 2 of the missense mutations resulted in kinetic abnormalities of the receptor and 1 was kinetically benign. One patient was an 11-year-old male who had decreased move-



ments in utero, a weak cry and a feeble suck at birth, ptosis of the eyelids beginning at 5 months of age, and ophthalmoparesis beginning at 2 years of age. He always fatigued easily, could never run well, and had difficulty climbing steps. The nonsense mutation in this patient was a 190C–T transition that converted an arginine codon to a TGA stop codon at position 64 (R64X) of the CHRNE gene. The mutated arginine is conserved across epsilon subunits of other species, but not in other subunits. The other mutation in the CHRNE gene was a 440G–T transversion that predicted to result in an R147L amino acid substitution (100725.0005). Since this transversion altered a nucleotide at the end of exon 5, aberrant splicing was sought but not detected. An affected brother had both mutations; the asymptomatic mother had the R64X allele and the asymptomatic father and brother had the R147L allele.

[67446] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67447] Ohno, K.; Quiram, P. A.; Milone, M.; Wang, H.–L.; Harper, M. C.; Pruitt, J. N., II; Brengman, J. M.; Pao, L.; Fischbeck, K. H.; Crawford, T. O.; Sine, S. M.; Engel, A. G. : Congenital

myasthenic syndromes due to heteroallelic nonsense/mis-sense mutations in the acetylcholine receptor epsilon subunit gene: identification and functional characterization of six new mutations. Hum. Molec. Genet. 6: 753–766, 1997.  
; and

[67448] Witzemann, V.; Schwarz, H.; Koenen, M.; Berberich, C.; Villarroel, A.; Wernig, A.; Brenner, H. R.; Sakmann, B. : Acetylcholine receptor epsilon-subunit deletion causes muscle weakness a.

[67449] Further studies establishing the function and utilities of CHRNE are found in John Hopkins OMIM database record ID 100725, and in cited publications numbered 4113–24 and 11575–4119 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. 2',3'-cyclic Nucleotide 3' Phosphodiesterase (CNP, Accession NM\_033133) is another VGAM1959 host target gene. CNP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNP BINDING SITE, designated SEQ ID:26977, to the nucleotide sequence of VGAM1959 RNA, herein

designated VGAM RNA, also designated SEQ ID:4670.

[67450] Another function of VGAM1959 is therefore inhibition of 2',3'-cyclic Nucleotide 3' Phosphodiesterase (CNP, Accession NM\_033133), a gene which can link tubulin to membranes and may regulate cytoplasmic microtubule distribution. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNP. The function of CNP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM443. Contactin 2 (axonal) (CNTN2, Accession NM\_005076) is another VGAM1959 host target gene. CNTN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNTN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNTN2 BINDING SITE, designated SEQ ID:11526, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67451] Another function of VGAM1959 is therefore inhibition of Contactin 2 (axonal) (CNTN2, Accession NM\_005076), a

gene which may play a role in axonal growth and cell adhesion. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNTN2. The function of CNTN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259. Collagen, Type I, Alpha 1 (COL1A1, Accession NM\_000088) is another VGAM1959 host target gene. COL1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL1A1 BINDING SITE, designated SEQ ID:5540, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67452] Another function of VGAM1959 is therefore inhibition of Collagen, Type I, Alpha 1 (COL1A1, Accession NM\_000088). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL1A1. COX11 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX11,

Accession NM\_004375) is another VGAM1959 host target gene. COX11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by COX11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX11 BINDING SITE, designated SEQ ID:10594, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67453] Another function of VGAM1959 is therefore inhibition of COX11 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX11, Accession NM\_004375). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX11. Collapsin Response Mediator Protein 1 (CRMP1, Accession NM\_001313) is another VGAM1959 host target gene. CRMP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CRMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRMP1 BINDING SITE, des-

ignated SEQ ID:6999, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67454] Another function of VGAM1959 is therefore inhibition of Collapsin Response Mediator Protein 1 (CRMP1, Accession NM\_001313), a gene which is a member of dihydropyrimidinase family. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRMP1. The function of CRMP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1146. Chemokine (C-X-C motif) Ligand 16 (CXCL16, Accession NM\_022059) is another VGAM1959 host target gene. CXCL16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXCL16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXCL16 BINDING SITE, designated SEQ ID:22597, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67455] Another function of VGAM1959 is therefore inhibition of Chemokine (C-X-C motif) Ligand 16 (CXCL16, Accession NM\_022059), a gene which induces calcium mobilization. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXCL16. The function of CXCL16 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1845.

Chromosome X Open Reading Frame 6 (CXorf6, Accession NM\_005491) is another VGAM1959 host target gene. CXorf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXorf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXorf6 BINDING SITE, designated SEQ ID:11991, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67456] Another function of VGAM1959 is therefore inhibition of Chromosome X Open Reading Frame 6 (CXorf6, Accession NM\_005491). Accordingly, utilities of VGAM1959 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with CXorf6. Drebrin 1 (DBN1, Accession NM\_080881) is another VGAM1959 host target gene. DBN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DBN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DBN1 BINDING SITE, designated SEQ ID:28123, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67457] Another function of VGAM1959 is therefore inhibition of Drebrin 1 (DBN1, Accession NM\_080881). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DBN1. Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM\_096398) is another VGAM1959 host target gene. DLG5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DLG5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLG5 BINDING SITE, designated SEQ ID:40335,



to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67458] Another function of VGAM1959 is therefore inhibition of Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM\_096398), a gene which may transmit extracellular signals to inhibit cell proliferation. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLG5. The function of DLG5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM444. Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM\_004013) is another VGAM1959 host target gene. DMD BINDING SITE1 through DMD BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DMD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMD BINDING SITE1 through DMD BINDING SITE3, designated SEQ ID:10192, SEQ ID:10219 and SEQ ID:10231 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4670.

[67459] Another function of VGAM1959 is therefore inhibition of Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM\_004013), a gene which muscular dystrophy . Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMD. The function of DMD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM218.DXS1283E (Accession XM\_047871) is another VGAM1959 host target gene. DXS1283E BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DXS1283E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DXS1283E BINDING SITE, designated SEQ ID:35061, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67460] Another function of VGAM1959 is therefore inhibition of DXS1283E (Accession XM\_047871). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with DXS1283E. Ephrin-B1 (EFNB1, Accession NM\_004429) is another VGAM1959 host target gene. EFNB1 BINDING SITE1 and EFNB1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by EFNB1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNB1 BINDING SITE1 and EFNB1 BINDING SITE2, designated SEQ ID:10710 and SEQ ID:10711 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67461] Another function of VGAM1959 is therefore inhibition of Ephrin-B1 (EFNB1, Accession NM\_004429), a gene which is a transmembrane ligand of Eph-related receptor tyrosine kinases, has a role in cell adhesion. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNB1. The function of EFNB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM390.Egl Nine Homolog 2 (*C. elegans*)

(EGLN2, Accession NM\_017555) is another VGAM1959 host target gene. EGLN2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGLN2 BINDING SITE, designated SEQ ID:18992, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67462] Another function of VGAM1959 is therefore inhibition of Egl Nine Homolog 2 (*C. elegans*) (EGLN2, Accession NM\_017555), a gene which is an essential component of the pathway. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGLN2. The function of EGLN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM432. Enoyl-Coenzyme A, Hydratase/3-hydroxyacyl Coenzyme A Dehydrogenase (EHHADH, Accession NM\_001966) is another VGAM1959 host target gene. EHHADH BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by EHHADH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EHHADH BINDING SITE, designated SEQ ID:7695, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67463] Another function of VGAM1959 is therefore inhibition of Enoyl-Coenzyme A, Hydratase/3-hydroxyacyl Coenzyme A Dehydrogenase (EHHADH, Accession NM\_001966), a gene which functions in the peroxisomal beta-oxidation pathway. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EHHADH. The function of EHHADH has been established by previous studies. Hoefler et al. (1994) reported the full-length cDNA sequence of the enoyl-CoA-hydratase:3-hydroxyacyl-CoA dehydrogenase bifunctional enzyme. The cDNA sequence spans 3,779 nucleotides with an open reading frame of 2,169 nucleotides. Animal model experiments lend further support to the function of EHHADH. Qi et al. (1999) generated Lpb null mice. Mutant mice were viable and fertile and ex-

hibited no detectable gross phenotypic defects. The only defect was a blunting of peroxisome proliferative response upon challenge with a peroxisome proliferator. The absence of appreciable changes in lipid metabolism indicated that enoyl-CoAs, generated in the classical system in Lpb null mice, were diverted to the D-hydroxy-specific system for metabolism by Dpb (OMIM Ref. No. 601860).

[67464] It is appreciated that the abovementioned animal model for EHHADH is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[67465] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67466] Hoefler, G.; Forstner, M.; McGuinness, M. C.; Hulla, W.; Hidden, M.; Krisper, P.; Kenner, L.; Ried, T.; Lengauer, C.; Zechner, R.; mOser, H. W.; Chen, G. L. : cDNA cloning of the human peroxisomal enoyl-CoA hydratase:3-hydroxyacyl-CoA dehydrogenase bifunctional enzyme and localization to chromosome 3q26.3-3q28: a free left Alu arm is inserted in the 3-prime noncoding region. Genomics 19: 60-67, 1994. ; and

[67467] Qi, C.; Zhu, Y.; Pan, J.; Usuda, N.; Maeda, N.; Yeldandi, A. V.; Rao, M. S.; Hashimoto, T.; Reddy, J. K. : Absence of spontaneous peroxisome proliferation in enoyl-CoA hydratase/L-3-hyd.

[67468] Further studies establishing the function and utilities of EHHADH are found in John Hopkins OMIM database record ID 607037, and in cited publications numbered 5170 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ELAV (embryonic lethal, abnormal vision, *Drosophila*)-like 3 (Hu antigen C) (ELAVL3, Accession NM\_001420) is another VGAM1959 host target gene. ELAVL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELAVL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELAVL3 BINDING SITE, designated SEQ ID:7119, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67469] Another function of VGAM1959 is therefore inhibition of ELAV (embryonic lethal, abnormal vision, *Drosophila*)-like 3 (Hu antigen C) (ELAVL3, Accession NM\_001420), a gene

which arises when an immune response to systemic tumors expressing neuronal proteins develops into an autoimmune neuronal degeneration. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELAVL3. The function of ELAVL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM883. Endonuclease G (ENDOG, Accession NM\_004435) is another VGAM1959 host target gene. ENDOG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ENDOG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENDOG BINDING SITE, designated SEQ ID:10720, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67470] Another function of VGAM1959 is therefore inhibition of Endonuclease G (ENDOG, Accession NM\_004435), a gene which cleaves double and single stranded dna. also has ribonuclease (rnase) and rnase h activities. capable of gen-



erating the rna primers required to initiate replication of mitochondrial dna . Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENDOG. The function of ENDOG has been established by previous studies. Tiranti et al. (1995) mapped 3 human housekeeping genes involved in mitochondrial biogenesis. One of these was the gene encoding a mitochondrion-specific endonuclease, designated ENDOG, that preferentially cleaves DNA stretches rich in C and G residues. The authors hypothesized that this endonuclease could play a role in the maturation of RNA complementary stretches serving as primers for mtDNA replication, in the splicing process of polycistronic transcripts, or in mtDNA repair. By PCR-based screening of a somatic cell hybrid panel and by fluorescence in situ hybridization, Tiranti et al. (1995) assigned the ENDOG locus to 9q34.1. Li et al. (2001) identified endoG as the nuclease specifically activated by apoptotic stimuli and able to induce nucleosomal fragmentation of DNA in fibroblast cells from embryonic mice lacking DFF45 (OMIM Ref. No. 601882). EndoG is a mitochondrion-specific nuclease that translocates to the nucleus during apoptosis. Once released from mitochondria, en-

doG cleaves chromatin DNA into nucleosomal fragments independently of caspases (see OMIM Ref. No. 147678). Therefore, ENDOG represents a caspase-independent apoptotic pathway initiated from the mitochondria. In *C. elegans*, Parrish et al. (2001) found that reduction of activity of cps6, a homolog of ENDOG, affected normal DNA degradation and resulted in delayed appearance of cell corpses during development. This observation provided in vivo evidence that the DNA degradation process is important for proper progression of apoptosis. Parrish et al. (2001) stated that CPS6 is the first mitochondrial protein identified to be involved in programmed cell death in *C. elegans*, underscoring the conserved and important role of mitochondria in the execution of apoptosis

[67471] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67472] Li, L. Y.; Luo, X.; Wang, X. : Endonuclease G is an apoptotic DNase when released from mitochondria. *Nature* 412: 95–99, 2001. ; and

[67473] Parrish, J.; Li, L.; Klotz, K.; Ledwich, D.; Wang, X.; Xue, D. : Mitochondrial endonuclease G is important for apoptosis in *C. elegans*. *Nature* 412: 90–94, 2001.

[67474] Further studies establishing the function and utilities of ENDOG are found in John Hopkins OMIM database record ID 600440, and in cited publications numbered 7707–770 and 7706 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Epidermal Growth Factor Receptor Pathway Substrate 15 (EPS15, Accession NM\_001981) is another VGAM1959 host target gene. EPS15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPS15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPS15 BINDING SITE, designated SEQ ID:7712, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67475] Another function of VGAM1959 is therefore inhibition of Epidermal Growth Factor Receptor Pathway Substrate 15 (EPS15, Accession NM\_001981), a gene which involved in cell growth regulation. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPS15. The function of EPS15 has been established by previous studies.

Fazioli et al. (1993) developed an expression cloning approach which, applied to the study of epidermal growth factor receptor (EGFR)-activated signaling, yielded a number of murine cDNA clones, referred to as eps (for egfr-pathway-substrate) clones. One of these clones, eps15, encoded a protein of 140 to 150 kD which was phosphorylated on tyrosine following activation of the EGFR (OMIM Ref. No. 131550) and platelet-derived growth factor receptor (PDGFR; 173410). Phosphorylation of eps15 appeared relatively receptor-specific since the erbB-2 receptor (OMIM Ref. No. 164870), which is highly related to EGFR, was not able to phosphorylate it efficiently. Wong et al. (1994) cloned the human homolog and mapped the EPS15 gene to 1p32-p31 by analysis of human/rodent hybrids retaining various segments of human chromosome 1. The region of assignment is one involved in deletion in neuroblastoma, translocations in acute lymphoblastic leukemia, and a fragile site. Most of the translocations affecting the chromosome band 11q23 in human acute leukemias involve a restricted area of the HRX gene, also known as MLL for myeloid/lymphoid, or mixed-lineage leukemia (OMIM Ref. No. 159555). Other partners in the fused gene created by the translocation in-

clude AF4 (OMIM Ref. No. 159557) on chromosome 4, AF9 (OMIM Ref. No. 159558) on chromosome 9, and ENL (OMIM Ref. No. 159556) on chromosome 19. Indeed, at least 15 different chromosomal partners have been involved with MLL (also known as ALL1) in leukemia-producing translocations. In 2 myeloid leukemias, the derivative chromosome 11 expressed the 1368 N-terminal amino acids MLL fused to almost all the AF1P product. The predicted wildtype AF1P product was a 98-kD acidic protein that exhibited no similarity to AF4, AF9, and ENL gene products. It was highly similar to the murine EPS15 gene product. Bernard et al. (1994) characterized 2 t(1;11)(p32;q11) translocations that fused the MML gene to a novel gene, tentatively designated AF1P, on 1p32. Their AF1P is clearly the same gene as EPS15.

[67476] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67477] Fazioli, F.; Minichiello, L.; Matoska, V.; Castagnino, P.; Miki, T.; Wong, W. T.; Di Fiore, P. P. : Eps8, a substrate for the epidermal growth factor receptor kinase, enhances EGF-dependent mitogenic signals. EMBO J. 12: 3799–3808, 1993. ; and

[67478] Bernard, O. A.; Mauchauffe, M.; Mecucci, C.; Van Den Berghe, H.; Berger, R. : A novel gene, AF-1p, fused to HRX in t(1;11)(p32;q23), is not related to AF-4, AF-9 nor ENL. Oncogene 9: 103.

[67479] Further studies establishing the function and utilities of EPS15 are found in John Hopkins OMIM database record ID 600051, and in cited publications numbered 7726–7730 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ets Variant Gene 5 (ets-related molecule) (ETV5, Accession NM\_004454) is another VGAM1959 host target gene. ETV5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ETV5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ETV5 BINDING SITE, designated SEQ ID:10750, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67480] Another function of VGAM1959 is therefore inhibition of Ets Variant Gene 5 (ets-related molecule) (ETV5, Accession NM\_004454), a gene which DNA binding protein of the Ets oncoprotein family. Accordingly, utilities of VGAM1959

include diagnosis, prevention and treatment of diseases and clinical conditions associated with ETV5. The function of ETV5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM1171. Ellis Van Creveld Syndrome (EVC, Accession NM\_014556) is another VGAM1959 host target gene. EVC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EVC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVC BINDING SITE, designated SEQ ID:15896, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67481] Another function of VGAM1959 is therefore inhibition of Ellis Van Creveld Syndrome (EVC, Accession NM\_014556). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVC. Exostoses (multiple) 1 (EXT1, Accession NM\_000127) is another VGAM1959 host target gene. EXT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

EXT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXT1 BINDING SITE, designated SEQ ID:5603, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67482] Another function of VGAM1959 is therefore inhibition of Exostoses (multiple) 1 (EXT1, Accession NM\_000127). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXT1. Enhancer of Zeste Homolog 1 (Drosophila) (EZH1, Accession NM\_001991) is another VGAM1959 host target gene. EZH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EZH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EZH1 BINDING SITE, designated SEQ ID:7718, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67483] Another function of VGAM1959 is therefore inhibition of Enhancer of Zeste Homolog 1 (Drosophila) (EZH1, Acces-



sion NM\_001991), a gene which may act in transcriptional regulation and heterochromatin maintenance. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EZH1. The function of EZH1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM251. Fanconi Anemia, Complement Group F (FANCF, Accession NM\_022725) is another VGAM1959 host target gene. FANCF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FANCF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FANCF BINDING SITE, designated SEQ ID:22921, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67484] Another function of VGAM1959 is therefore inhibition of Fanconi Anemia, Complement Group F (FANCF, Accession NM\_022725). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FANCF. Fatty Acid

Synthase (FASN, Accession NM\_004104) is another VGAM1959 host target gene. FASN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FASN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FASN BINDING SITE, designated SEQ ID:10316, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67485] Another function of VGAM1959 is therefore inhibition of Fatty Acid Synthase (FASN, Accession NM\_004104), a gene which catalyzes the formation of long-chain fatty acids from acetyl-coa, malonyl-coa and nadph. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FASN. The function of FASN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM477. Fibroblast Growth Factor 23 (FGF23, Accession NM\_020638) is another VGAM1959 host target gene. FGF23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FGF23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF23 BINDING SITE, designated SEQ ID:21792, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67486] Another function of VGAM1959 is therefore inhibition of Fibroblast Growth Factor 23 (FGF23, Accession NM\_020638), a gene which is a member of the fibroblast growth factor family . Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF23. The function of FGF23 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM24. Filamin B, Beta (actin binding protein 278) (FLNB, Accession XM\_030806) is another VGAM1959 host target gene. FLNB BINDING SITE1 and FLNB BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLNB, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementar-

ity of the nucleotide sequences of FLNB BINDING SITE1 and FLNB BINDING SITE2, designated SEQ ID:31140 and SEQ ID:31141 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67487] Another function of VGAM1959 is therefore inhibition of Filamin B, Beta (actin binding protein 278) (FLNB, Accession XM\_030806), a gene which Filamin B, beta; binds actin, interacts with cytoplasmic domain of Ibalpha. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLNB. The function of FLNB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM416. Follistatin-like 3 (secreted glycoprotein) (FSTL3, Accession NM\_005860) is another VGAM1959 host target gene. FSTL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FSTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FSTL3 BINDING SITE, designated SEQ ID:12468, to the nucleotide se-

quence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67488] Another function of VGAM1959 is therefore inhibition of Follistatin-like 3 (secreted glycoprotein) (FSTL3, Accession NM\_005860), a gene which is a member of the follistatin-module-protein family. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FSTL3. The function of FSTL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.FXYD Domain Containing Ion Transport Regulator 6 (FXYD6, Accession NM\_022003) is another VGAM1959 host target gene. FXYD6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FXYD6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FXYD6 BINDING SITE, designated SEQ ID:22553, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67489] Another function of VGAM1959 is therefore inhibition of

FXYP Domain Containing Ion Transport Regulator 6 (FXYP6, Accession NM\_022003). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FXYP6. Giant Axonal Neuropathy (gigaxonin) (GAN, Accession NM\_022041) is another VGAM1959 host target gene. GAN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAN BINDING SITE, designated SEQ ID:22566, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67490] Another function of VGAM1959 is therefore inhibition of Giant Axonal Neuropathy (gigaxonin) (GAN, Accession NM\_022041), a gene which plays an important role in neurofilament architecture. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAN. The function of GAN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM606. GATA Binding Protein 2 (GATA2, Accession NM\_002050) is another VGAM1959 host target gene. GATA2 BINDING SITE1 and GATA2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GATA2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GATA2 BINDING SITE1 and GATA2 BINDING SITE2, designated SEQ ID:7803 and SEQ ID:7807 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67491] Another function of VGAM1959 is therefore inhibition of GATA Binding Protein 2 (GATA2, Accession NM\_002050). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GATA2. Glyoxalase I (GLO1, Accession NM\_006708) is another VGAM1959 host target gene. GLO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of GLO1 BINDING SITE, designated SEQ ID:13528, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67492] Another function of VGAM1959 is therefore inhibition of Glyoxalase I (GLO1, Accession NM\_006708), a gene which converts methylglyoxal and glutathione to S-lactoylglutathione. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLO1. The function of GLO1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM786. Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 3 (GNAI3, Accession NM\_006496) is another VGAM1959 host target gene. GNAI3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAI3 BINDING SITE, designated SEQ ID:13242, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ



ID:4670.

[67493] Another function of VGAM1959 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 3 (GNAI3, Accession NM\_006496), a gene which stimulates receptor regulated K<sup>+</sup>-channels. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAI3. The function of GNAI3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM45.G Protein-coupled Receptor 44 (GPR44, Accession NM\_004778) is another VGAM1959 host target gene. GPR44 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR44, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR44 BINDING SITE, designated SEQ ID:11176, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67494] Another function of VGAM1959 is therefore inhibition of G

Protein-coupled Receptor 44 (GPR44, Accession NM\_004778), a gene which mediates signals to the interior of the cell via activation of heterotrimeric G proteins . Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR44. The function of GPR44 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1669. G Protein-coupled Receptor Kinase 7 (GPRK7, Accession NM\_139209) is another VGAM1959 host target gene. GPRK7 BINDING SITE1 and GPRK7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GPRK7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPRK7 BINDING SITE1 and GPRK7 BINDING SITE2, designated SEQ ID:29227 and SEQ ID:29230 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67495] Another function of VGAM1959 is therefore inhibition of G Protein-coupled Receptor Kinase 7 (GPRK7, Accession

NM\_139209), a gene which may play a role in signal transduction pathways that involve calcium as a second messenger. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPRK7. The function of GPRK7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM640. Histone Deacetylase 4 (HDAC4, Accession NM\_006037) is another VGAM1959 host target gene. HDAC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HDAC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC4 BINDING SITE, designated SEQ ID:12661, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67496] Another function of VGAM1959 is therefore inhibition of Histone Deacetylase 4 (HDAC4, Accession NM\_006037), a gene which is responsible for the deacetylation of lysine residues on the n-terminal part of the core histones and

may mediate transcriptional regulation. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC4. The function of HDAC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM264. Histone Deacetylase 7A (HDAC7A, Accession NM\_015401) is another VGAM1959 host target gene. HDAC7A BINDING SITE1 and HDAC7A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HDAC7A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC7A BINDING SITE1 and HDAC7A BINDING SITE2, designated SEQ ID:17714 and SEQ ID:18684 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67497] Another function of VGAM1959 is therefore inhibition of Histone Deacetylase 7A (HDAC7A, Accession NM\_015401). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC7A. Interferon (alpha, beta and

omega) Receptor 2 (IFNAR2, Accession NM\_000874) is another VGAM1959 host target gene. IFNAR2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IFNAR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IFNAR2 BINDING SITE, designated SEQ ID:6555, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67498] Another function of VGAM1959 is therefore inhibition of Interferon (alpha, beta and omega) Receptor 2 (IFNAR2, Accession NM\_000874), a gene which is a receptor for interferons alpha and beta. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IFNAR2. The function of IFNAR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM487. Insulin-like Growth Factor Binding Protein 5 (IGFBP5, Accession NM\_000599) is another VGAM1959 host target gene. IGFBP5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA

encoded by IGFBP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGFBP5 BINDING SITE, designated SEQ ID:6203, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67499] Another function of VGAM1959 is therefore inhibition of Insulin-like Growth Factor Binding Protein 5 (IGFBP5, Accession NM\_000599), a gene which either inhibits or stimulates the growth promoting effects of the igfs on cell culture. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGFBP5. The function of IGFBP5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1233. Interleukin 2 Receptor, Beta (IL2RB, Accession NM\_000878) is another VGAM1959 host target gene. IL2RB BINDING SITE1 and IL2RB BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by IL2RB, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL2RB BINDING SITE1 and IL2RB BINDING SITE2, designated SEQ ID:6571 and SEQ ID:6572 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67500] Another function of VGAM1959 is therefore inhibition of Interleukin 2 Receptor, Beta (IL2RB, Accession NM\_000878), a gene which is involved in receptor mediated endocytosis and transduces the mitogenic signals of il-2. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL2RB. The function of IL2RB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM450. IRTA1 (Accession NM\_031282) is another VGAM1959 host target gene. IRTA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRTA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRTA1 BINDING SITE, designated SEQ ID:25305,

to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67501] Another function of VGAM1959 is therefore inhibition of IRTA1 (Accession NM\_031282). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRTA1. Immunoglobulin Superfamily Containing Leucine-rich Repeat (ISLR, Accession NM\_005545) is another VGAM1959 host target gene. ISLR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ISLR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ISLR BINDING SITE, designated SEQ ID:12073, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67502] Another function of VGAM1959 is therefore inhibition of Immunoglobulin Superfamily Containing Leucine-rich Repeat (ISLR, Accession NM\_005545). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ISLR. IL2-inducible T-cell Kinase (ITK, Accession



NM\_005546) is another VGAM1959 host target gene. ITK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITK BINDING SITE, designated SEQ ID:12075, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67503] Another function of VGAM1959 is therefore inhibition of IL2-inducible T-cell Kinase (ITK, Accession NM\_005546), a gene which plays a role in t cell proliferation and differentiation. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITK. The function of ITK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM288. Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224) is another VGAM1959 host target gene. ITPR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR3, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR3 BINDING SITE, designated SEQ ID:8001, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67504] Another function of VGAM1959 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM\_002224), a gene which may be responsible for calcium release from intracellular stores. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR3. The function of ITPR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM310. Intersectin 1 (SH3 domain protein) (ITSN1, Accession NM\_003024) is another VGAM1959 host target gene. ITSN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITSN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITSN1 BINDING SITE, designated SEQ ID:8958, to the nucleotide sequence of VGAM1959 RNA,

herein designated VGAM RNA, also designated SEQ ID:4670.

[67505] Another function of VGAM1959 is therefore inhibition of Intersectin 1 (SH3 domain protein) (ITSN1, Accession NM\_003024), a gene which may be involved in endocytosis and synaptic vesicle recycling. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITSN1. The function of ITSN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1233. Potassium Inwardly-rectifying Channel, Subfamily J, Member 10 (KCNJ10, Accession NM\_002241) is another VGAM1959 host target gene. KCNJ10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNJ10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ10 BINDING SITE, designated SEQ ID:8026, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67506] Another function of VGAM1959 is therefore inhibition of

Potassium Inwardly-rectifying Channel, Subfamily J, Member 10 (KCNJ10, Accession NM\_002241), a gene which may be responsible for potassium buffering action of glial cells in the brain. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ10. The function of KCNJ10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM167. Potassium Channel, Subfamily K, Member 1 (KCNK1, Accession NM\_002245) is another VGAM1959 host target gene. KCNK1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNK1 BINDING SITE, designated SEQ ID:8033, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67507] Another function of VGAM1959 is therefore inhibition of Potassium Channel, Subfamily K, Member 1 (KCNK1, Accession NM\_002245), a gene which is an inward rectifying

potassium channel. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNK1. The function of KCNK1 has been established by previous studies. Potassium channels are functionally important to a large number of cellular processes including maintenance of the action potential, muscle contraction, hormone secretion, osmotic regulation, and ion flow. Lesage et al. (1996) cloned a member of a new class of potassium channels by computer identification of an EST with predicted sequence similarity to the P domain (a region involved in the potassium conduction pathway) of previously known channels. A cDNA, designated TWIK1 by the authors, was obtained from a human kidney library and shown to encode a predicted 336-amino acid protein. Unlike other potassium channels, TWIK1 has 4 (rather than 6) transmembrane domains and 2 (rather than 1) P domains. Two genes from *C. elegans* are related. When expressed in *Xenopus* oocytes, TWIK1 is able to direct expression of weakly inward-rectifying potassium currents. Northern blots showed that the gene is transcribed in a large number of tissues but is especially highly expressed in the brain and heart. The authors speculated that TWIK1 channels may be involved

in the control of background potassium membrane conductances. Lesage et al. (1996) mapped the gene by in situ hybridization to 1q42–q43.

[67508] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67509] Lesage, F.; Guillemare, E.; Fink, M.; Duprat, F.; Lazdunski, M.; Romey, G.; Barhanin, J. : TWIK–1, a ubiquitous human weakly inward rectifying K<sup>+</sup> channel with a novel structure. EMBO J. 15: 1004–1011, 1996. ; and

[67510] Lesage, F.; Mattei, M.–G.; Fink, M.; Barhanin, J.; Lazdunski, M. : Assignment of the human weak inward rectifier K<sup>+</sup> channel TWIK–1 gene to chromosome 1q42–q43. Genomics 34: 153–155, 1996.

[67511] Further studies establishing the function and utilities of KCNK1 are found in John Hopkins OMIM database record ID 601745, and in cited publications numbered 6203–6204 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Potassium Channel, Subfamily K, Member 5 (KCNK5, Accession NM\_003740) is another VGAM1959 host target gene. KCNK5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

KCNK5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNK5 BINDING SITE, designated SEQ ID:9829, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67512] Another function of VGAM1959 is therefore inhibition of Potassium Channel, Subfamily K, Member 5 (KCNK5, Accession NM\_003740). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNK5. Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 2 (KCNS2, Accession XM\_043106) is another VGAM1959 host target gene. KCNS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNS2 BINDING SITE, designated SEQ ID:33901, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67513] Another function of VGAM1959 is therefore inhibition of Potassium Voltage-gated Channel, Delayed-rectifier, Sub-family S, Member 2 (KCNS2, Accession XM\_043106), a gene which mediates the voltage-dependent potassium ion permeability of excitable membranes. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNS2. The function of KCNS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM419. Kinase Insert Domain Receptor (a type III receptor tyrosine kinase) (KDR, Accession NM\_002253) is another VGAM1959 host target gene. KDR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KDR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KDR BINDING SITE, designated SEQ ID:8053, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67514] Another function of VGAM1959 is therefore inhibition of Kinase Insert Domain Receptor (a type III receptor tyrosine



kinase) (KDR, Accession NM\_002253). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KDR. KIAA0857 (Accession XM\_039552) is another VGAM1959 host target gene. KIAA0857 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0857, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0857 BINDING SITE, designated SEQ ID:33121, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67515] Another function of VGAM1959 is therefore inhibition of KIAA0857 (Accession XM\_039552), a gene which is involved in cytoskeletal organization and cellular growth. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0857. The function of KIAA0857 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM548.Kinesin Family Member 5C (KIF5C, Accession

NM\_004522) is another VGAM1959 host target gene.

KIF5C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF5C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF5C BINDING SITE, designated SEQ ID:10854, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67516] Another function of VGAM1959 is therefore inhibition of Kinesin Family Member 5C (KIF5C, Accession NM\_004522). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF5C. Kinesin Family Member C3 (KIFC3, Accession NM\_005550) is another VGAM1959 host target gene. KIFC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIFC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIFC3 BINDING SITE, designated SEQ ID:12081, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4670.

[67517] Another function of VGAM1959 is therefore inhibition of Kinesin Family Member C3 (KIFC3, Accession NM\_005550), a gene which may function in intracellular transport and mitosis. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIFC3. The function of KIFC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1006. Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession NM\_002293) is another VGAM1959 host target gene. LAMC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAMC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMC1 BINDING SITE, designated SEQ ID:8078, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67518] Another function of VGAM1959 is therefore inhibition of Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession

NM\_002293), a gene which may mediate the attachment, migration, and organization of cells into tissues. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAMC1. The function of LAMC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM812. Lamin B Receptor (LBR, Accession XM\_001795) is another VGAM1959 host target gene. LBR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LBR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LBR BINDING SITE, designated SEQ ID:29854, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67519] Another function of VGAM1959 is therefore inhibition of Lamin B Receptor (LBR, Accession XM\_001795). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LBR. Lunatic Fringe Homolog (Drosophila) (LFNG, Accession XM\_166539) is another VGAM1959 host target

gene. LFNG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LFNG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LFNG BINDING SITE, designated SEQ ID:44509, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67520] Another function of VGAM1959 is therefore inhibition of Lunatic Fringe Homolog (Drosophila) (LFNG, Accession XM\_166539). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LFNG. Leukemia Inhibitory Factor (cholinergic differentiation factor) (LIF, Accession NM\_002309) is another VGAM1959 host target gene. LIF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIF BINDING SITE, designated SEQ ID:8095, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67521] Another function of VGAM1959 is therefore inhibition of Leukemia Inhibitory Factor (cholinergic differentiation factor) (LIF, Accession NM\_002309). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIF. Leukemia Inhibitory Factor Receptor (LIFR, Accession NM\_002310) is another VGAM1959 host target gene. LIFR BINDING SITE1 and LIFR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LIFR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIFR BINDING SITE1 and LIFR BINDING SITE2, designated SEQ ID:8104 and SEQ ID:8106 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67522] Another function of VGAM1959 is therefore inhibition of Leukemia Inhibitory Factor Receptor (LIFR, Accession NM\_002310). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIFR. Lymphotoxin Beta (TNF superfamily, member 3) (LTB, Accession NM\_009588)

is another VGAM1959 host target gene. LTB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LTB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LTB BINDING SITE, designated SEQ ID:14315, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67523] Another function of VGAM1959 is therefore inhibition of Lymphotoxin Beta (TNF superfamily, member 3) (LTB, Accession NM\_009588). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LTB. Mannose-6-phosphate Receptor (cation dependent) (M6PR, Accession NM\_002355) is another VGAM1959 host target gene. M6PR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by M6PR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of M6PR BINDING SITE, designated SEQ ID:8164, to the nucleotide sequence of VGAM1959 RNA, herein

designated VGAM RNA, also designated SEQ ID:4670.

[67524] Another function of VGAM1959 is therefore inhibition of Mannose-6-phosphate Receptor (cation dependent) (M6PR, Accession NM\_002355), a gene which is involved in intracellular sorting and transport of acid hydrolases. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with M6PR. The function of M6PR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1924. MAD, Mothers Against Decapentaplegic Homolog 5 (Drosophila) (MADH5, Accession NM\_005903) is another VGAM1959 host target gene. MADH5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MADH5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADH5 BINDING SITE, designated SEQ ID:12523, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67525] Another function of VGAM1959 is therefore inhibition of



MAD, Mothers Against Decapentaplegic Homolog 5 (Drosophila) (MADH5, Accession NM\_005903), a gene which is a transcriptional modulator activated by bmp (bone morphogenetic proteins) type 1 receptor kinase. smad5 is a receptor-regulated smad (r-smad). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADH5. The function of MADH5 has been established by previous studies. Gemma et al. (1998) determined the full-length cDNA sequence of human MADH5, which they called SMAD5. Comparison of the cDNA sequence with the SMAD5 genomic sequence, obtained from YAC clones, showed that the SMAD5 gene has 8 exons, with the coding sequence contained in exons 3 to 8. By 5-prime RACE, the authors identified a SMAD5 cDNA derived from an alternatively spliced transcript that lacks the 75-bp exon 2. Using PCR-SSCP analysis to investigate the frequency of SMAD5 somatic mutations in human cancers, Gemma et al. (1998) did not detect either homozygous deletions or point mutations in 40 primary gastric tumors or 51 cell lines derived from diverse types of cancer, including 20 cell lines resistant to the growth inhibitory effects of TGF-beta. The SMAD5 protein has strong homol-

ogy with SMAD1 (OMIM Ref. No. 601595), SMAD2 (OMIM Ref. No. 601366), SMAD3 (OMIM Ref. No. 603109), and SMAD4 (OMIM Ref. No. 600993) in the N- and C-terminal domains, which are separated by a proline-rich sequence; SMAD5 shows the greatest homology to SMAD1. Bruno et al. (1998) showed that SMAD5 plays a critical role in the signaling pathway by which TGF-beta inhibits the proliferation of human hematopoietic progenitor cells.

[67526] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67527] Bruno, E.; Horrigan, S. K.; Van Den Berg, D.; Rozler, E.; Fitting, P. R.; Moss, S. T.; Westbrook, C.; Hoffman, R. : The Smad5 gene is involved in the intracellular signaling pathways that mediate the inhibitory effects of transforming growth factor-beta on human hematopoiesis. Blood 91: 1917-1923, 1998. ; and

[67528] Riggins, G. J.; Thiagalingam, S.; Rozenblum, E.; Weinstein, C. L.; Kern, S. E.; Hamilton, S. R.; Willson, J. K. V.; Markowitz, S. D.; Kinzler, K. W.; Vogelstein, B. : Mad-related genes in t.

[67529] Further studies establishing the function and utilities of MADH5 are found in John Hopkins OMIM database record

ID 603110, and in cited publications numbered 8582–858 and 6480 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mastermind-like 1 (Drosophila) (MAML1, Accession NM\_014757) is another VGAM1959 host target gene. MAML1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAML1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAML1 BINDING SITE, designated SEQ ID:16497, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67530] Another function of VGAM1959 is therefore inhibition of Mastermind-like 1 (Drosophila) (MAML1, Accession NM\_014757), a gene which MAML1 functions as a transcriptional coactivator for Notch signaling. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAML1. The function of MAML1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM556. Microtubule-associated Protein 1A (MAP1A, Accession NM\_002373) is another VGAM1959 host target gene. MAP1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP1A BINDING SITE, designated SEQ ID:8187, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67531] Another function of VGAM1959 is therefore inhibition of Microtubule-associated Protein 1A (MAP1A, Accession NM\_002373), a gene which is a structural protein involved in the filamentous cross-bridging between microtubules and other skeletal elements. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP1A. The function of MAP1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM315. Methyl-CpG Binding Domain Protein 3 (MBD3, Accession NM\_003926) is another VGAM1959 host

target gene. MBD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBD3 BINDING SITE, designated SEQ ID:10018, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67532] Another function of VGAM1959 is therefore inhibition of Methyl-CpG Binding Domain Protein 3 (MBD3, Accession NM\_003926), a gene which are subunits of the NURD (nucleosome remodeling and histone deacetylase) complex. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBD3. The function of MBD3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Myelin Basic Protein (MBP, Accession XM\_117096) is another VGAM1959 host target gene. MBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBP, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBP BINDING SITE, designated SEQ ID:43221, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67533] Another function of VGAM1959 is therefore inhibition of Myelin Basic Protein (MBP, Accession XM\_117096), a gene which Myelin basic protein; a constituent of myelin, plays a role in nerve function. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBP. The function of MBP has been established by previous studies. Eosinophil granule major basic protein (MBP) comprises the crystalloid core of the eosinophil granule. Wasmoen et al. (1988) and Weller et al. (1988) published a partial amino acid sequence for MBP, also designated proteoglycan-2 (PRG2). Using this partial sequence, Barker et al. (1988) isolated a full-length PRG2 cDNA from a human promyelocytic leukemia cell line (HL60) cDNA library. McGrogan et al. (1988) independently isolated a PRG2 cDNA from an HL60 cell line cDNA. Yoshimatsu et al. (1992) also identified PRG2 in a search for a natural killer (NK) cell-

activating factor purified from the supernatant of a T-cell hybridoma. McGrogan et al. (1988) and Barker et al. (1988) determined that the PRG2 cDNA encodes a deduced 222-amino acid protein with a 15-amino acid hydrophobic signal sequence. PRG2 is initially translated as a 25-kD preproprotein that is posttranslationally modified to a proprotein. Posttranslational modification results in the mature form of PRG2, which is encoded by the carboxy 117 amino acids of the preproprotein and has a molecular mass of 14 kD. The 90-amino acid N-terminal domain has 1 potential N-linked glycosylation site. Yoshimatsu et al. (1992) reported that the C-terminal end of PRG2 shares homology with animal lectins. McGrogan et al. (1988) determined that the putative PRG2 proprotein is a bipolar molecule. The amino-terminal half is hydrophilic, whereas the mature PRG2 is hydrophobic. Barker et al. (1988) hypothesized that the translation of PRG2 as a bipolar proprotein may mask the toxic effects of the mature PRG2 and protect the eosinophil from damage while the protein is processed through the endoplasmic reticulum to its sequestered site in the eosinophil granule. Using Northern blot analysis, McGrogan et al. (1988) detected a major 1-kb transcript and a minor

0.5-kb PRG2 transcript in HL60 cells. By the same method, Li et al. (1995) detected a 1-kb transcript in immature cells including bone-marrow and HL60 cells, but not in purified blood eosinophils. Using RT-PCR, Li et al. (1995) detected an additional 1.6-kb transcript in bone marrow cells and HL60 cells at lower levels than the 1-kb transcript. In differentiated blood eosinophils from idiopathic hypereosinophilic syndrome patients, the 1.6-kb transcript predominated. The International Radiation Hybrid Mapping Consortium mapped the PRG2 gene to chromosome 11 (A005W41). By FISH, Plager et al. (2001) mapped the PRG2 and PRG3 (OMIM Ref. No. 606814) genes to chromosome 11cen-q12. Animal model experiments lend further support to the function of MBP.

[67534] It is appreciated that the abovementioned animal model for MBP is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[67535] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67536] Li, M.-S.; Sun, L.; Satoh, T.; Fisher, L. M.; Spry, C. J. F. : Human eosinophil major basic protein, a mediator of al-



lergic inflammation, is expressed by alternative splicing from two promoters. Biochem. J. 305: 921–927, 1995. ; and

[67537] Plager, D. A.; Weiler, D. A.; Loegering, D. A.; Johnson, W. B.; Haley, L.; Eddy, R. L.; Shows, T. B.; Gleich, G. J. : Comparative structure, proximal promoter elements, and chromosome lo.

[67538] Further studies establishing the function and utilities of MBP are found in John Hopkins OMIM database record ID 605601, and in cited publications numbered 6995–7001 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. MADS Box Transcription Enhancer Factor 2, Polypeptide C (myocyte enhancer factor 2C) (MEF2C, Accession NM\_002397) is another VGAM1959 host target gene. MEF2C BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MEF2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEF2C BINDING SITE, designated SEQ ID:8214, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67539] Another function of VGAM1959 is therefore inhibition of MADS Box Transcription Enhancer Factor 2, Polypeptide C (myocyte enhancer factor 2C) (MEF2C, Accession NM\_002397), a gene which regulates muscle-specific and mitogen-inducible genes. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEF2C. The function of MEF2C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM386. MADS Box Transcription Enhancer Factor 2, Polypeptide D (myocyte enhancer factor 2D) (MEF2D, Accession XM\_173049) is another VGAM1959 host target gene. MEF2D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEF2D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEF2D BINDING SITE, designated SEQ ID:46307, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67540] Another function of VGAM1959 is therefore inhibition of

MADS Box Transcription Enhancer Factor 2, Polypeptide D (myocyte enhancer factor 2D) (MEF2D, Accession XM\_173049), a gene which regulates muscle-specific and mitogen-inducible genes. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEF2D. The function of MEF2D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1306. Methyltransferase-like 1 (METTL1, Accession NM\_023032) is another VGAM1959 host target gene. METTL1 BINDING SITE1 and METTL1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by METTL1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of METTL1 BINDING SITE1 and METTL1 BINDING SITE2, designated SEQ ID:23307 and SEQ ID:23312 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67541] Another function of VGAM1959 is therefore inhibition of Methyltransferase-like 1 (METTL1, Accession

NM\_023032). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with METTL1. Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession NM\_015166) is another VGAM1959 host target gene. MLC1 BINDING SITE1 and MLC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MLC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLC1 BINDING SITE1 and MLC1 BINDING SITE2, designated SEQ ID:17523 and SEQ ID:29217 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67542] Another function of VGAM1959 is therefore inhibition of Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession NM\_015166). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLC1. Mature T-cell Proliferation 1 (MTCP1, Accession NM\_014221) is another VGAM1959 host target gene. MTCP1 BINDING SITE is HOST TARGET binding site found

in the 5` untranslated region of mRNA encoded by MTCP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTCP1 BINDING SITE, designated SEQ ID:15486, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67543] Another function of VGAM1959 is therefore inhibition of Mature T-cell Proliferation 1 (MTCP1, Accession NM\_014221). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTCP1. Myotubularin Related Protein 8 (MTMR8, Accession NM\_015458) is another VGAM1959 host target gene. MTMR8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MTMR8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR8 BINDING SITE, designated SEQ ID:17747, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67544] Another function of VGAM1959 is therefore inhibition of Myotubularin Related Protein 8 (MTMR8, Accession NM\_015458), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTMR8. The function of MTMR8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM379. Mevalonate Kinase (mevalonic aciduria) (MVK, Accession XM\_027151) is another VGAM1959 host target gene. MVK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MVK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MVK BINDING SITE, designated SEQ ID:30425, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67545] Another function of VGAM1959 is therefore inhibition of Mevalonate Kinase (mevalonic aciduria) (MVK, Accession XM\_027151). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with MVK. N-acetylgalactosaminidase, Alpha- (NAGA, Accession NM\_000262) is another VGAM1959 host target gene. NAGA BINDING SITE1 and NAGA BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NAGA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAGA BINDING SITE1 and NAGA BINDING SITE2, designated SEQ ID:5799 and SEQ ID:5802 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67546] Another function of VGAM1959 is therefore inhibition of N-acetylgalactosaminidase, Alpha- (NAGA, Accession NM\_000262). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAGA. Niemann-Pick Disease, Type C1 (NPC1, Accession NM\_000271) is another VGAM1959 host target gene. NPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPC1 BINDING SITE, designated SEQ ID:5814, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67547] Another function of VGAM1959 is therefore inhibition of Niemann–Pick Disease, Type C1 (NPC1, Accession NM\_000271). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPC1. Neuronal Pentraxin II (NPTX2, Accession XM\_166492) is another VGAM1959 host target gene. NPTX2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NPTX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPTX2 BINDING SITE, designated SEQ ID:44425, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67548] Another function of VGAM1959 is therefore inhibition of Neuronal Pentraxin II (NPTX2, Accession XM\_166492), a gene which is likely to play role in the modification of cel–



lular properties that underlie long-term plasticity. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPTX2. The function of NPTX2 has been established by previous studies. Pentraxins constitute a family of proteins that include C-reactive protein (CRP; 123260) and serum amyloid P protein (APCS; 104770). Hsu and Perin (1995) noted that the prototypic pentraxin, C-reactive protein, was first identified as a serum component that binds *Streptococcus pneumoniae* (Tillett and Francis, 1930 and Abernethy and Avery, 1941) and whose serum concentration increases up to 1,000-fold during an acute phase response. Pentraxins acquired their name from their ability to form pentameric (or decameric) complexes and have been characterized by their ability to bind numerous ligands. The latter property raises the possibility that these proteins may mediate a nonspecific uptake of bacteria and cell debris that may be associated with inflammation and immune responses. Schlimgen et al. (1995) identified a novel neuronal pentraxin in rat as a potential receptor mediating the uptake of the presynaptic snake venom toxin taipoxin (see OMIM Ref. No. NPTX1, 602367). Based on the low identity to other pentraxins

and the hypothesis that this neuronal pentraxin may mediate uptake of degraded synaptic material, Hsu and Perin (1995) sought to identify additional members of what they suspected represents a new family of pentraxins. They reported the cDNA and genomic sequences of a second neuronal pentraxin in humans, for which they proposed the name neuronal pentraxin II (NPTX2). They found that it shows 54% amino acid identity to rat neuronal pentraxin I, with 69% identity over the carboxy-terminal half of NP I, and is 88% identical to a sperm acrosomal pentraxin. Northern blot analysis demonstrated that NPTX2 message is present in brain, testis, pancreas, liver, heart, and skeletal muscle; thus, unlike NP I, NP II is not exclusively localized to neurons. Like NP I, NP II has potential N-linked glycosylation sites. The human NPTX2 gene is 11 kb long and contains 4 introns. By fluorescence in situ hybridization, Hsu and Perin (1995) mapped the NPTX2 gene to 7q21.3–q22.1.

[67549] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67550] Hsu, Y.-C.; Perin, M. S. : Human neuronal pentraxin II (NPTX2): conservation, genomic structure, and chromoso-

mal localization. Genomics 28: 220–227, 1995. ; and

[67551] Schlimgen, A. K.; Helms, J. A.; Vogel, H.; Perin, M. S. :  
Neuronal pentraxin, a secreted protein with homology to  
acute phase proteins of the immune system. Neuron 14:  
519–526, 1995.

[67552] Further studies establishing the function and utilities of  
NPTX2 are found in John Hopkins OMIM database record  
ID 600750, and in cited publications numbered 3786,  
7571–757 and 3787 listed in the bibliography section  
hereinbelow, which are also hereby incorporated by refer-  
ence. Nuclear Receptor Subfamily 3, Group C, Member 2  
(NR3C2, Accession NM\_000901) is another VGAM1959  
host target gene. NR3C2 BINDING SITE is HOST TARGET  
binding site found in the 3` untranslated region of mRNA  
encoded by NR3C2, corresponding to a HOST TARGET  
binding site such as BINDING SITE I, BINDING SITE II or  
BINDING SITE III. Table 2 illustrates the complementarity  
of the nucleotide sequences of NR3C2 BINDING SITE, des-  
ignated SEQ ID:6595, to the nucleotide sequence of  
VGAM1959 RNA, herein designated VGAM RNA, also des-  
ignated SEQ ID:4670.

[67553] Another function of VGAM1959 is therefore inhibition of  
Nuclear Receptor Subfamily 3, Group C, Member 2

(NR3C2, Accession NM\_000901), a gene which is to increase ion and water transport and thus raise extracellular fluid volume and blood pressure and lower potassium levels. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR3C2. The function of NR3C2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM186.Nebulin-related Anchoring Protein (Nrap, Accession NM\_139235) is another VGAM1959 host target gene. Nrap BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Nrap, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Nrap BINDING SITE, designated SEQ ID:29239, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67554] Another function of VGAM1959 is therefore inhibition of Nebulin-related Anchoring Protein (Nrap, Accession NM\_139235), a gene which performs an anchoring function to link the terminal actin filaments of myofibrils to

protein complexes located beneath the sarcolemma. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Nrap. The function of Nrap and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM649. Nuclear Receptor Interacting Protein 1 (NRIP1, Accession XM\_009699) is another VGAM1959 host target gene. NRIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRIP1 BINDING SITE, designated SEQ ID:30121, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67555] Another function of VGAM1959 is therefore inhibition of Nuclear Receptor Interacting Protein 1 (NRIP1, Accession XM\_009699), a gene which modulates transcriptional activation by the estrogen receptor. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRIP1.

The function of NRIP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM276.8-oxoguanine DNA Glycosylase (OGG1, Accession NM\_016819) is another VGAM1959 host target gene. OGG1 BINDING SITE1 through OGG1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OGG1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OGG1 BINDING SITE1 through OGG1 BINDING SITE3, designated SEQ ID:18811, SEQ ID:18816 and SEQ ID:8394 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67556] Another function of VGAM1959 is therefore inhibition of 8-oxoguanine DNA Glycosylase (OGG1, Accession NM\_016819), a gene which is involved in base excision DNA repair and removal of 8-oxyguanine. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OGG1. The function of OGG1 and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM390. Oncostatin M (OSM, Accession NM\_020530) is another VGAM1959 host target gene. OSM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSM BINDING SITE, designated SEQ ID:21754, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67557] Another function of VGAM1959 is therefore inhibition of Oncostatin M (OSM, Accession NM\_020530), a gene which inhibits the proliferation of a number of tumor cell lines, caused an acute inflammatory reaction. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSM. The function of OSM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1078. Pyrimidinergic Receptor P2Y, G-protein Coupled, 6 (P2RY6, Accession NM\_004154) is another VGAM1959 host target gene. P2RY6 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P2RY6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RY6 BINDING SITE, designated SEQ ID:10355, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67558] Another function of VGAM1959 is therefore inhibition of Pyrimidinergic Receptor P2Y, G-protein Coupled, 6 (P2RY6, Accession NM\_004154), a gene which mediates cellular responses to nucleotides. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RY6. The function of P2RY6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM445. Protocadherin 11 X-linked (PCDH11X, Accession NM\_032968) is another VGAM1959 host target gene. PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH11X, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING



SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2, designated SEQ ID:26795 and SEQ ID:26810 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67559] Another function of VGAM1959 is therefore inhibition of Protocadherin 11 X-linked (PCDH11X, Accession NM\_032968), a gene which is thought to play a fundamental role in cell-cell recognition essential for the segmental development and function of the central nervous system. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH11X. The function of PCDH11X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433. Protocadherin 11 Y-linked (PCDH11Y, Accession NM\_032973) is another VGAM1959 host target gene. PCDH11Y BINDING SITE1 and PCDH11Y BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH11Y, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING

SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH11Y BINDING SITE1 and PCDH11Y BINDING SITE2, designated SEQ ID:26829 and SEQ ID:9851 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67560] Another function of VGAM1959 is therefore inhibition of Protocadherin 11 Y-linked (PCDH11Y, Accession NM\_032973). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH11Y. Prohibitin (PHB, Accession NM\_002634) is another VGAM1959 host target gene. PHB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHB BINDING SITE, designated SEQ ID:8494, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67561] Another function of VGAM1959 is therefore inhibition of Prohibitin (PHB, Accession NM\_002634). Accordingly, utilities of VGAM1959 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with PHB. PIG8 (Accession NM\_004879) is another VGAM1959 host target gene. PIG8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIG8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIG8 BINDING SITE, designated SEQ ID:11315, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67562] Another function of VGAM1959 is therefore inhibition of PIG8 (Accession NM\_004879), a gene which is induced by p53 and may be involved in apoptosis. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIG8. The function of PIG8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM737. Phosphoinositide-3-kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM\_002646) is another VGAM1959 host target gene. PIK3C2B BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by PIK3C2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3C2B BINDING SITE, designated SEQ ID:8509, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67563] Another function of VGAM1959 is therefore inhibition of Phosphoinositide-3-kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM\_002646). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3C2B. Polycystic Kidney Disease 1 (autosomal dominant) (PKD1, Accession NM\_000296) is another VGAM1959 host target gene. PKD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKD1 BINDING SITE, designated SEQ ID:5842, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67564] Another function of VGAM1959 is therefore inhibition of Polycystic Kidney Disease 1 (autosomal dominant) (PKD1, Accession NM\_000296). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKD1. Phosphomannomutase 2 (PMM2, Accession XM\_050755) is another VGAM1959 host target gene. PMM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMM2 BINDING SITE, designated SEQ ID:35679, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67565] Another function of VGAM1959 is therefore inhibition of Phosphomannomutase 2 (PMM2, Accession XM\_050755). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMM2. Peroxisome Proliferative Activated Receptor, Gamma, Coactivator 1 (PPARGC1, Accession NM\_013261) is another VGAM1959 host target gene. PPARGC1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by PPARGC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPARGC1 BINDING SITE, designated SEQ ID:14932, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67566] Another function of VGAM1959 is therefore inhibition of Peroxisome Proliferative Activated Receptor, Gamma, Coactivator 1 (PPARGC1, Accession NM\_013261), a gene which may play a role in insulin sensitivity and thermogenesis. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPARGC1. The function of PPARGC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM952. Peptidyl-prolyl Isomerase G (cyclophilin G) (PPIG, Accession NM\_004792) is another VGAM1959 host target gene. PPIG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPIG, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPIG BINDING SITE, designated SEQ ID:11202, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67567] Another function of VGAM1959 is therefore inhibition of Peptidyl–prolyl Isomerase G (cyclophilin G) (PPIG, Accession NM\_004792), a gene which catalyzes the cis–trans isomerization of proline imidic peptide bonds in oligopeptides. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPIG. The function of PPIG has been established by previous studies. The peptidyl–prolyl cis/trans isomerase protein family (PPIases) includes the cyclophilin, FK506–binding protein (e.g., FKBP1A; 186945), and parvulin (e.g., PIN4, 300252) subfamilies. The cyclophilins have been implicated in the folding, transport, and assembly of proteins. Using a yeast 2–hybrid screen to identify proteins that interact with Clk (CLK1; 601951), Nestel et al. (1996) isolated partial clones of a mouse gene, which they called CARS–Cyp. By screening a thymus cDNA library with the mouse clone, they as–

sembled a full-length cDNA of the human homolog, PPIG. Using a yeast 2-hybrid screen to identify proteins that interact with the phosphorylated C-terminal domain (CTD) of the largest subunit of RNA polymerase II (POLR2A; 180660), Bourquin et al. (1997) independently cloned PPIG, which they called SRcyp/CASP10, from a B-lymphocyte cDNA library. PPIG is predicted to encode a 754-amino acid protein containing 2 Nopp140 (nucleolar phosphoprotein of 140 kD)-related domains and a large C-terminal serine/arginine (SR)-rich domain found predominantly in pre-mRNA splicing factors. The N-terminal region of PPIG contains a peptidyl-prolyl cis-trans isomerase domain characteristic of immunophilins/cyclophilins. PPIG shares 37.8% sequence identity with NKTR (OMIM Ref. No. 161565), a myeloid-specific nuclear protein. By Northern blot analysis, Nestel et al. (1996) detected PPIG expression at similar levels in lung, liver, kidney, small intestine, testis, and brain. They detected major 4-kb and minor 10-kb PPIG transcripts in human B-cell RNA. Although PPIG was widely expressed, it appeared to be absent from NK cells. By Northern blot analysis, Bourquin et al. (1997) detected a broadly expressed single 3.0-kb PPIG transcript. Using deletion mutant analysis,



Bourquin et al. (1997) determined that the SR domain of PPIG is required for interaction with the CTD of POLR2A in yeast 2-hybrid assays. Using GST fusion proteins, they confirmed that PPIG directly interacts with the CTD. Using immunostaining, they demonstrated that PPIG is distributed in nuclear speckles, a nuclear compartment rich in splicing factors, and colocalizes with the splicing factor SC35 (SFRS2; 600813). They concluded that PPIG may be a component of splicing factor complexes that bind the CTD, thereby linking RNA processing to transcription.

[67568] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67569] Bourquin, J.-P.; Stagljar, I.; Meier, P.; Moosmann, P.; Silke, J.; Baechi, T.; Georgiev, O.; Schaffner, W. : A serine/arginine-rich nuclear matrix cyclophilin interacts with the C-terminal domain of RNA polymerase II. *Nucleic Acids Res.* 25: 2055-2061, 1997. ; and

[67570] Nestel, F. P.; Colwill, K.; Harper, S.; Pawson, T.; Anderson, S. K. : RS cyclophilins: identification of an NK-TR(1)-related cyclophilin. *Gene* 180: 151-155, 1996.

[67571] Further studies establishing the function and utilities of PPIG are found in John Hopkins OMIM database record ID

606093, and in cited publications numbered 12399 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PR Domain Containing 4 (PRDM4, Accession NM\_012406) is another VGAM1959 host target gene. PRDM4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRDM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM4 BINDING SITE, designated SEQ ID:14785, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67572] Another function of VGAM1959 is therefore inhibition of PR Domain Containing 4 (PRDM4, Accession NM\_012406). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM4. PRex1 (Accession NM\_020820) is another VGAM1959 host target gene. PRex1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRex1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of PRex1 BINDING SITE, designated SEQ ID:21885, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67573] Another function of VGAM1959 is therefore inhibition of PRex1 (Accession NM\_020820). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRex1. Prokineticin 1 (PROK1, Accession NM\_032414) is another VGAM1959 host target gene. PROK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PROK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROK1 BINDING SITE, designated SEQ ID:26199, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67574] Another function of VGAM1959 is therefore inhibition of Prokineticin 1 (PROK1, Accession NM\_032414), a gene which induces proliferation, migration and fenestration in capillary endothelial cells derived from endocrine glands.

Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROK1. The function of PROK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1000. Prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy) (PSAP, Accession XM\_045140) is another VGAM1959 host target gene. PSAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSAP BINDING SITE, designated SEQ ID:34373, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67575] Another function of VGAM1959 is therefore inhibition of Prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy) (PSAP, Accession XM\_045140). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSAP. Prostaglandin F2 Re-

ceptor Negative Regulator (PTGFRN, Accession XM\_040709) is another VGAM1959 host target gene. PTGFRN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGFRN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGFRN BINDING SITE, designated SEQ ID:33363, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67576] Another function of VGAM1959 is therefore inhibition of Prostaglandin F2 Receptor Negative Regulator (PTGFRN, Accession XM\_040709), a gene which inhibits the binding of prostaglandin f2-alpha (pgf2- alpha) to its specific fp receptor. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGFRN. The function of PTGFRN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125.Prostaglandin-endoperoxide Synthase 1 (prostaglandin G/H synthase and cyclooxygenase) (PTGS1,

Accession NM\_080591) is another VGAM1959 host target gene. PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTGS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2, designated SEQ ID:27901 and SEQ ID:6680 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67577] Another function of VGAM1959 is therefore inhibition of Prostaglandin-endoperoxide Synthase 1 (prostaglandin G/H synthase and cyclooxygenase) (PTGS1, Accession NM\_080591), a gene which may play an important role in regulating or promoting cell proliferation in some normal and neoplastically transformed cells. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGS1. The function of PTGS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. Protein Tyrosine Phosphatase,

Receptor Type, G (PTPRG, Accession NM\_002841) is another VGAM1959 host target gene. PTPRG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTPRG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRG BINDING SITE, designated SEQ ID:8726, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67578] Another function of VGAM1959 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, G (PTPRG, Accession NM\_002841), a gene which is a candidate tumor suppressor and represents a subfamily of receptor tyrosine phosphatases. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRG. The function of PTPRG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1924.RAD9 Homolog (*S. pombe*) (RAD9, Accession NM\_004584) is another VGAM1959 host target gene. RAD9 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by RAD9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD9 BINDING SITE, designated SEQ ID:10932, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67579] Another function of VGAM1959 is therefore inhibition of RAD9 Homolog (*S. pombe*) (RAD9, Accession NM\_004584), a gene which may function as a cell cycle checkpoint protein. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD9. The function of RAD9 has been established by previous studies. In *S. pombe*, rad9 is one of 6 genes essential for both the incomplete DNA replication (S-M) and DNA damage checkpoints. See HUS1 (OMIM Ref. No. 603760). By searching an EST database, Lieberman et al. (1996) identified a partial cDNA encoding HRAD9, a human rad9 homolog. The authors used the partial cDNA to recover additional human RAD9 cDNAs corresponding to the entire coding region. The predicted 391-amino acid human protein is 25% identical to *S. pombe* rad9. The human RAD9 gene par-



tially complemented the hydroxyurea sensitivity, radiosensitivity, and checkpoint defects of rad9-null mutant cells. On immunoblots of mammalian cell extracts, Volkmer and Karnitz (1999) found that human RAD9 migrated at 70 kD, even though it has a predicted molecular mass of 45 kD. The authors attributed this discrepancy to complex posttranslational modifications. In vivo, the human RAD9 protein was phosphorylated in response to DNA damage, suggesting that it participates in a DNA damage-inducible signaling pathway. Immunoprecipitation studies demonstrated that the fully modified form of RAD9 interacts selectively with RAD1 (OMIM Ref. No. 603153) and HUS1 in a stable complex. Volkmer and Karnitz (1999) concluded that these 3 proteins are central components of a DNA damage-responsive protein complex in human cells.

[67580] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67581] Lieberman, H. B.; Hopkins, K. M.; Nass, M.; Demetrick, D.; Davey, S. : A human homolog of the *Schizosaccharomyces pombe* rad9+ checkpoint control gene. *Proc. Nat. Acad. Sci.* 93: 13890–13895, 1996. ; and

[67582] Volkmer, E.; Karnitz, L. M. : Human homologs of Schizosaccharomyces pombe Rad1, Hus1, and Rad9 form a DNA damage-responsive protein complex. J. Biol. Chem. 274: 567–570, 1999.

[67583] Further studies establishing the function and utilities of RAD9 are found in John Hopkins OMIM database record ID 603761, and in cited publications numbered 7626 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RalA Binding Protein 1 (RALBP1, Accession NM\_006788) is another VGAM1959 host target gene. RALBP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RALBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RALBP1 BINDING SITE, designated SEQ ID:13659, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67584] Another function of VGAM1959 is therefore inhibition of RalA Binding Protein 1 (RALBP1, Accession NM\_006788), a gene which plays a role in signal transduction and catalyzes the transport of glutathione conjugates and xeno-

biotics. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RALBP1. The function of RALBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM345. RAN Binding Protein 3 (RANBP3, Accession NM\_007321) is another VGAM1959 host target gene. RANBP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RANBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RANBP3 BINDING SITE, designated SEQ ID:14237, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67585] Another function of VGAM1959 is therefore inhibition of RAN Binding Protein 3 (RANBP3, Accession NM\_007321). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RANBP3. Ras Association (RalGDS/AF-6) Domain Family 1 (RASSF1, Accession NM\_007182) is another VGAM1959 host target gene.

RASSF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASSF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASSF1 BINDING SITE, designated SEQ ID:14038, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67586] Another function of VGAM1959 is therefore inhibition of Ras Association (RalGDS/AF-6) Domain Family 1 (RASSF1, Accession NM\_007182), a gene which is a candidate renal tumor suppressor. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASSF1. The function of RASSF1 has been established by previous studies. Allelic loss at the short arm of chromosome 3 is one of the most common and earliest events in the pathogenesis of lung cancer, and is observed in more than 90% of small cell lung cancers (SCLCs) and in 50 to 80% of non-small cell lung cancers (OMIM Ref. No. NSCLCs). Frequent and early loss of heterozygosity and the presence of homozygous deletions suggested a critical role of the region 3p21.3 in

tumorigenesis, and a region of common homozygous deletion in 3p21.3 was narrowed to 120 kb by Sekido et al. (1998). Several putative tumor-suppressor genes located at 3p21 had been characterized, but none of these appeared to be altered in lung cancer. Dammann et al. (2000) described the cloning and characterization of a human RAS effector homolog, RASSF1, located in the 120-kb region of minimal homozygous deletion. They identified the RASSF1 protein through its interaction with the human DNA repair protein XPA (OMIM Ref. No. 278700) in a yeast 2-hybrid screen. Dammann et al. (2000) detected 3 transcripts, A, B, and C, derived from alternative splicing and promoter usage. The major transcripts A and C were expressed in all normal tissues tested. Transcript A was missing in all SCLC cell lines analyzed and in several other cancer cell lines. Loss of expression was correlated with methylation of the CpG island promoter sequence of RASSF1A. The promoter was highly methylated in 24 of 60 (40%) primary lung tumors, and 4 of 41 tumors analyzed carried missense mutations. Reexpression of transcript A in lung carcinoma cells reduced colony formation, suppressed anchorage-independent growth, and inhibited tumor formation in nude mice. These characteristics indi-

cated a potential role for RASSF1A as a lung tumor suppressor. Dammann et al. (2000) found no mutations in 17 SCLC cell lines, but found 4 missense mutations in 41 primary NSCLCs.

[67587] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67588] Dammann, R.; Li, C.; Yoon, J.-H.; Chin, P. L.; Bates, S.; Pfeifer, G. P. : Epigenetic inactivation of a RAS association domain family protein from the lung tumour suppressor locus 3p21.3. *Nature Genet.* 25: 315–319, 2000. ; and

[67589] Sekido, Y.; Ahmadian, M.; Wistuba, I. I.; Latif, F.; Bader, S.; Wei, M.-H.; Duh, F.-M.; Gazdar, A. F.; Lerman, M. I.; Minna, J. D. : Cloning of a breast cancer homozygous deletion jun.

[67590] Further studies establishing the function and utilities of RASSF1 are found in John Hopkins OMIM database record ID 605082, and in cited publications numbered 6597–6599, 10 and 6600 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Retinoblastoma Binding Protein 5 (RBBP5, Accession NM\_005057) is another VGAM1959 host target gene. RBBP5 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by RBBP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBBP5 BINDING SITE, designated SEQ ID:11486, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67591] Another function of VGAM1959 is therefore inhibition of Retinoblastoma Binding Protein 5 (RBBP5, Accession NM\_005057). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBBP5. Regulator of Non-sense Transcripts 1 (RENT1, Accession NM\_002911) is another VGAM1959 host target gene. RENT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RENT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RENT1 BINDING SITE, designated SEQ ID:8814, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67592] Another function of VGAM1959 is therefore inhibition of Regulator of Nonsense Transcripts 1 (RENT1, Accession NM\_002911), a gene which eliminates the production of nonsense-containing RNAs in mammalian cells. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RENT1. The function of RENT1 has been established by previous studies. Sun et al. (1998) provided evidence for a factor that functions to eliminate the production of nonsense-containing RNAs in mammalian cells. They identified the factor, variously referred to as RENT1 and HUPF1, by isolating cDNA for a human homolog of *S. cerevisiae* Upf1p, which is a group I RNA helicase that functions in the nonsense-mediated decay of mRNA in yeast. Using monkey COS cells and human HeLa cells, Sun et al. (1998) demonstrated that expression of human Upf1 protein harboring an arginine-to-cysteine mutation at residue 844 within the RNA helicase domain acts in a dominant-negative fashion to abrogate the decay of nonsense-containing mRNA that takes place in association with nuclei or in the cytoplasm. These findings provided evidence that nonsense-mediated mRNA decay is related mechanistically in yeast and in mammalian cells, regard-



less of the cellular site of decay. Animal model experiments lend further support to the function of RENT1. Medghalchi et al. (2001) explored the consequences of loss of NMRD function in vertebrates through targeted disruption of the *Rent1* gene, which encodes a mammalian ortholog of Upf1p, in murine embryonic stem cells. Mice heterozygous for the targeted allele showed no apparent phenotypic abnormalities but homozygosity was never observed, demonstrating that *Rent1* is essential for embryonic viability. Homozygous targeted embryos showed complete loss of NMRD and were viable in the preimplantation period, but resorbed shortly after implantation. Furthermore, *Rent1*  $-/-$  blastocysts isolated at 3.5 days postcoitum underwent apoptosis in culture following a brief phase of cellular expansion. The authors hypothesized that NMRD is essential for mammalian cellular viability and supports a critical role for the pathway in the regulated expression of selected physiologic transcripts.

[67593] It is appreciated that the abovementioned animal model for RENT1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[67594] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [67595] Sun, X.; Perlick, H. A.; Dietz, H. C.; Maquat, L. E. : A mutated human homologue to yeast Upf1 protein has a dominant-negative effect on the decay of nonsense-containing mRNAs in mammalian cells. *Proc. Nat. Acad. Sci.* 95: 10009–10014, 1998. ; and
- [67596] Medghalchi, S. M.; Frischmeyer, P. A.; Mendell, J. T.; Kelly, A. G.; Lawler, A. M.; Dietz, H. C. : Rent1, a trans-effector of nonsense-mediated mRNA decay, is essential for mammalian em.
- [67597] Further studies establishing the function and utilities of RENT1 are found in John Hopkins OMIM database record ID 601430, and in cited publications numbered 9277–9282 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Regulator of G-protein Signalling 3 (RGS3, Accession NM\_144488) is another VGAM1959 host target gene. RGS3 BINDING SITE1 through RGS3 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RGS3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of RGS3 BINDING SITE1 through RGS3 BINDING SITE6, designated SEQ ID:29306, SEQ ID:29308, SEQ ID:28282, SEQ ID:28668, SEQ ID:19423 and SEQ ID:22088 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67598] Another function of VGAM1959 is therefore inhibition of Regulator of G-protein Signalling 3 (RGS3, Accession NM\_144488), a gene which negatively regulates G protein-coupled receptor signalling. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS3. The function of RGS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM404.RP42 (Accession NM\_020640) is another VGAM1959 host target gene. RP42 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RP42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP42 BINDING SITE, designated SEQ ID:21803, to the nucleotide sequence of

VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67599] Another function of VGAM1959 is therefore inhibition of RP42 (Accession NM\_020640), a gene which not clear yet. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP42. The function of RP42 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM47. Ribulose-5-phosphate-3-epimerase (RPE, Accession XM\_030834) is another VGAM1959 host target gene. RPE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPE BINDING SITE, designated SEQ ID:31153, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67600] Another function of VGAM1959 is therefore inhibition of Ribulose-5-phosphate-3-epimerase (RPE, Accession XM\_030834). Accordingly, utilities of VGAM1959 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with RPE. Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM\_005063) is another VGAM1959 host target gene. SCD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCD BINDING SITE, designated SEQ ID:11499, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67601] Another function of VGAM1959 is therefore inhibition of Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM\_005063), a gene which functions in the synthesis of unsaturated fatty acids. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCD. The function of SCD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM314. Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM\_114281) is an-

other VGAM1959 host target gene. SCN1A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SCN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN1A BINDING SITE, designated SEQ ID:42834, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67602] Another function of VGAM1959 is therefore inhibition of Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM\_114281). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN1A. Succinate Dehydrogenase Complex, Subunit D, Integral Membrane Protein (SDHD, Accession NM\_003002) is another VGAM1959 host target gene. SDHD BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SDHD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDHD BINDING SITE, designated SEQ ID:8896, to the nucleotide se-

quence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67603] Another function of VGAM1959 is therefore inhibition of Succinate Dehydrogenase Complex, Subunit D, Integral Membrane Protein (SDHD, Accession NM\_003002). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDHD. Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 5 (SERPINB5, Accession NM\_002639) is another VGAM1959 host target gene. SERPINB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERPINB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERPINB5 BINDING SITE, designated SEQ ID:8495, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67604] Another function of VGAM1959 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 5 (SERPINB5, Accession NM\_002639), a gene which may be a serpin serine pro-

tease inhibitor and suppresses tumor metastasis. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERPINB5. The function of SERPINB5 has been established by previous studies. The nucleotide 5-methylcytosine is involved in processes crucial to mammalian development, such as X-chromosome inactivation and gene imprinting. In addition, cytosine methylation may be involved in the establishment and maintenance of cell type-specific expression of developmentally regulated genes; however, it is difficult to identify clear examples of such genes, particularly in humans. Futscher et al. (2002) provided evidence that cytosine methylation of the maspin gene promoter controls, in part, normal cell type-specific SERPINB5 expression. In normal cells expressing SERPINB5, the SERPINB5 promoter is unmethylated and the promoter region has acetylated histones and an accessible chromatin structure. In contrast, normal cells that do not express SERPINB5 have a completely methylated SERPINB5 promoter with hypoacetylated histones, an inaccessible chromatin structure, and a transcriptional repression that is relieved by inhibition of DNA methylation. These findings indicated that cytosine methylation is important in



the establishment and maintenance of cell type–restricted gene expression. Zou et al. (1994) used subtractive hybridization and the 'differential display' method to identify candidate tumor suppressor genes that are defective in human breast carcinoma cells. These genes were identified initially by searching for mRNAs whose expression is reduced or absent in tumor cells compared with normal cells grown under similar conditions. Zou et al. (1994) reported the characteristics of one of the more than 30 genes so identified, a member of the serpin family of protease inhibitors which they termed maspin. A single 3.0–kb maspin mRNA was expressed in normal mammary epithelial cell strains, but not in most mammary tumor cell lines examined. Southern blot analysis of XbaI–restricted DNA from normal and tumor cells with a maspin cDNA probe revealed no gross structural alterations of the maspin gene in the tumor cells. This result suggested that the maspin gene is downregulated but not mutated in cancer cells. Transfection of mammary carcinoma cells with the maspin gene did not alter the growth properties of the cells in vitro, but reduced their ability to induce tumors and metastasize in nude mice and to invade through a basement membrane matrix in vitro. Analysis of human

breast cancer specimens demonstrated that loss of maspin expression occurred most frequently in advanced cancers. These results supported the hypothesis that maspin functions as a tumor suppressor.

[67605] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67606] Zou, Z.; Anisowicz, A.; Hendrix, M. J. C.; Thor, A.; Neveu, M.; Sheng, S.; Rafidi, K.; Seftor, E.; Sager, R. : Maspin, a serpin with tumor-suppressing activity in human mammary epithelial cells. Science 263: 526–529, 1994. ; and

[67607] Futscher, B. W.; Oshiro, M. M.; Wozniak, R. J.; Holtan, N.; Hanigan, C. L.; Duan, H.; Domann, F. E. : Role for DNA methylation in the control of cell type-specific maspin expression. Nat.

[67608] Further studies establishing the function and utilities of SERPINB5 are found in John Hopkins OMIM database record ID 154790, and in cited publications numbered 2962–2963, 36 and 2964 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Splicing Factor 1 (SF1, Accession NM\_004630) is another VGAM1959 host target gene. SF1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by SF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SF1 BINDING SITE, designated SEQ ID:11001, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67609] Another function of VGAM1959 is therefore inhibition of Splicing Factor 1 (SF1, Accession NM\_004630), a gene which is a transcriptional repressor and splicing factor. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SF1. The function of SF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM934. SH3-domain Binding Protein 2 (SH3BP2, Accession NM\_003023) is another VGAM1959 host target gene. SH3BP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP2

BINDING SITE, designated SEQ ID:8951, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67610] Another function of VGAM1959 is therefore inhibition of SH3-domain Binding Protein 2 (SH3BP2, Accession NM\_003023). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BP2. Single-minded Homolog 2 (Drosophila) (SIM2, Accession NM\_005069) is another VGAM1959 host target gene. SIM2 BINDING SITE1 and SIM2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SIM2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIM2 BINDING SITE1 and SIM2 BINDING SITE2, designated SEQ ID:11518 and SEQ ID:14311 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67611] Another function of VGAM1959 is therefore inhibition of Single-minded Homolog 2 (Drosophila) (SIM2, Accession NM\_005069), a gene which may be a master gene of cns development. Accordingly, utilities of VGAM1959 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with SIM2. The function of SIM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM369. Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM\_005628) is another VGAM1959 host target gene. SLC1A5 BINDING SITE1 and SLC1A5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC1A5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A5 BINDING SITE1 and SLC1A5 BINDING SITE2, designated SEQ ID:12144 and SEQ ID:9525 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67612] Another function of VGAM1959 is therefore inhibition of Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM\_005628). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A5. Solute Carrier Family 7 (cationic amino acid

transporter,  $\gamma^+$  system), Member 6 (SLC7A6, Accession NM\_003983) is another VGAM1959 host target gene. SLC7A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A6 BINDING SITE, designated SEQ ID:10133, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67613] Another function of VGAM1959 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter,  $\gamma^+$  system), Member 6 (SLC7A6, Accession NM\_003983), a gene which is involved in mediating amino acid transport. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A6. The function of SLC7A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM87.SRY (sex determining region Y)-box 12 (SOX12, Accession NM\_006943) is another VGAM1959 host target gene.

SOX12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOX12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX12 BINDING SITE, designated SEQ ID:13831, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67614] Another function of VGAM1959 is therefore inhibition of SRY (sex determining region Y)-box 12 (SOX12, Accession NM\_006943). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOX12. SRGAP2 (Accession XM\_059095) is another VGAM1959 host target gene. SRGAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRGAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRGAP2 BINDING SITE, designated SEQ ID:36879, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ

ID:4670.

[67615] Another function of VGAM1959 is therefore inhibition of SRGAP2 (Accession XM\_059095). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRGAP2. Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 1 (STAM, Accession NM\_003473) is another VGAM1959 host target gene. STAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAM BINDING SITE, designated SEQ ID:9542, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67616] Another function of VGAM1959 is therefore inhibition of Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 1 (STAM, Accession NM\_003473), a gene which is as an adaptor molecule involved in the downstream signaling of cytokine receptors. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated



with STAM. The function of STAM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM927. Suppressor of Ty 6 Homolog (*S. cerevisiae*) (SUPT6H, Accession XM\_017037) is another VGAM1959 host target gene. SUPT6H BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SUPT6H, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUPT6H BINDING SITE, designated SEQ ID:30293, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67617] Another function of VGAM1959 is therefore inhibition of Suppressor of Ty 6 Homolog (*S. cerevisiae*) (SUPT6H, Accession XM\_017037), a gene which may normally act to repress transcription at a variety of loci, and also plays a role in chromatin structure or assembly. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUPT6H. The function of SUPT6H has been established by previous studies. Chiang et al. (1996) isolated

and sequenced SUPT6H and Supt6h, the human and murine homologs of the *Saccharomyces cerevisiae* and *Caenorhabditis elegans* genes SPT6 and emb-5, respectively. The human and murine SPT6 homologs are virtually identical, as they share more than 98% identity and more than 99% similarity at the protein level. The derived amino acid sequences of these 2 genes predicted a 1,603-amino acid polypeptide in human and a 1,726-amino acid polypeptide in mouse, respectively. The proteins have a highly acidic 5-prime region, a degenerate SH2 domain, and a leucine zipper, features consistent with a nuclear protein that regulates transcription. Northern blotting revealed a 7.0-kb transcript that was expressed constitutively in both mouse and human. Chiang et al. (1996) commented that SUPT6H appears to be functionally analogous to SPT6 and emb-5 and may therefore regulate transcription through establishment or maintenance of chromatin structure. By PCR-based analysis of somatic cell hybrids and by fluorescence in situ hybridization, Chiang et al. (1996) mapped the human homolog to 17q11.2. Segre et al. (1995) detected a cDNA fragment from the Supt6h gene on a mouse YAC that also contained the 'nude' locus. Their data placed Supt6h approximately 100

kb from whn (OMIM Ref. No. 600838), which is located on mouse chromosome 11. Thus, the Supt6h gene was mapped to mouse chromosome 11B1, which exhibits extensive homology of synteny with proximal human 17q.

[67618] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67619] Chiang, P.-W.; Wang, S.; Smithivas, P.; Song, W.-J.; Rammamoorthy, S.; Hillman, J.; Puett, S.; Van Keuren, M. L.; Crombez, E.; Kumar, A.; Glover, T. W.; Miller, D. E.; Tsai, C.-H.; Blackburn, C. C.; Chen, X.-N.; Sun, Z.; Cheng, J.-F.; Korenberg, J. R.; Kurnit, D. M. : Identification and analysis of the human and murine putative chromatin structure regulator SUPT6H and Supt6h. Genomics 34: 328–333, 1996. ; and

[67620] Segre, J. A.; Nemhauser, J. L.; Taylor, B. A.; Nadeau, J. H.; Lander, E. S. : Positional cloning of the nude locus: genetic, physical and transcription maps of the region and mutations.

[67621] Further studies establishing the function and utilities of SUPT6H are found in John Hopkins OMIM database record ID 601333, and in cited publications numbered 9480–9481 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. TATA Box Binding Protein (TBP)–associated Factor, RNA Polymerase I, C, 110kDa (TAF1C, Accession NM\_005679) is another VGAM1959 host target gene. TAF1C BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TAF1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF1C BINDING SITE, designated SEQ ID:12237, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67622] Another function of VGAM1959 is therefore inhibition of TATA Box Binding Protein (TBP)–associated Factor, RNA Polymerase I, C, 110kDa (TAF1C, Accession NM\_005679), a gene which belongs to component of the RNA polymerase I and II SL1 transcription factor. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF1C. The function of TAF1C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. TAF7 RNA Polymerase II, TATA

Box Binding Protein (TBP)–associated Factor, 55kDa (TAF7, Accession NM\_005642) is another VGAM1959 host target gene. TAF7 BINDING SITE1 and TAF7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TAF7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF7 BINDING SITE1 and TAF7 BINDING SITE2, designated SEQ ID:12175 and SEQ ID:12177 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67623] Another function of VGAM1959 is therefore inhibition of TAF7 RNA Polymerase II, TATA Box Binding Protein (TBP)–associated Factor, 55kDa (TAF7, Accession NM\_005642), a gene which may function as a coactivator of transcription with some activators. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF7. The function of TAF7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1316. Transcription Factor 2, Hepatic; LF-B3;

Variant Hepatic Nuclear Factor (TCF2, Accession NM\_006481) is another VGAM1959 host target gene. TCF2 BINDING SITE1 and TCF2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCF2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF2 BINDING SITE1 and TCF2 BINDING SITE2, designated SEQ ID:13204 and SEQ ID:13205 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67624] Another function of VGAM1959 is therefore inhibition of Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM\_006481), a gene which probably binds to the inverted palindrome 5'-gttaatnattaac-3'. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF2. The function of TCF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM118. Transcription Factor 4 (TCF4, Accession

NM\_003199) is another VGAM1959 host target gene.

TCF4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TCF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF4 BINDING SITE, designated SEQ ID:9187, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67625] Another function of VGAM1959 is therefore inhibition of Transcription Factor 4 (TCF4, Accession NM\_003199), a gene which is a transcriptional activator; interacts with ITF1 (TCF3); and contains basic helix-loop-helix domain. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF4. The function of TCF4 has been established by previous studies. The high mobility group (HMG) box is a DNA-binding domain. TCF7 (OMIM Ref. No. 189908), also called TCF1, and LEF1 (OMIM Ref. No. 153245), also called TCF1-alpha, are human lymphoid transcription factors that contain a virtually identical HMG box. By PCR of human genomic DNA using degenerate oligonucleotides based on the HMG boxes of TCF7 and

LEF1, Castrop et al. (1992) identified the TCF7L1 (OMIM Ref. No. 604652) and TCF7L2 genes, which they called TCF3 and TCF4, respectively. TCF7L1 and TCF7L2 were not expressed in cells of the lymphoid lineage. The deduced amino acid sequences of the HMG boxes of TCF7L1, TCF7L2, and TCF7 show striking homology. The authors suggested the existence of a subfamily of TCF7-like HMG box-containing transcription factors. Animal model experiments lend further support to the function of TCF4. To study the physiologic role of Tcf4 (which is encoded by the Tcf7l2 gene), Korinek et al. (1998) disrupted Tcf7l2 by homologous recombination. The homozygous null mice died shortly after birth. A single histopathologic abnormality was observed. An apparently normal transition of intestinal endoderm into epithelium occurred at approximately embryonic day (E) 14.5. However, no proliferative compartments were maintained in the prospective crypt regions between the villi. As a consequence, the neonatal epithelium was composed entirely of differentiated, nondividing villus cells. Korinek et al. (1998) concluded that the genetic program controlled by Tcf7l2 maintains the crypt stem cells of the small intestine. The constitutive activity of Tcf4 in APC-deficient ep-



ithelial cells may contribute to their malignant transformation by maintaining stem cell characteristics.

[67626] It is appreciated that the abovementioned animal model for TCF4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[67627] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67628] Castrop, J.; van Norren, K.; Clevers, H. : A gene family of HMG-box transcription factors with homology to TCF-1. Nucleic Acids Res. 20: 611 only, 1992. ; and

[67629] Korinek, V.; Barker, N.; Moerer, P.; van Donselaar, E.; Huls, G.; Peters, P. J.; Clevers, H. : Depletion of epithelial stem-cell compartments in the small intestine of mice lacking Tcf-4.

[67630] Further studies establishing the function and utilities of TCF4 are found in John Hopkins OMIM database record ID 602228, and in cited publications numbered 5893-589 and 2303-2305 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. T-cell, Immune Regulator 1, ATPase, H<sup>+</sup> Transporting, Lysosomal V0 Protein A Isoform 3 (TCIRG1, Accession

NM\_006053) is another VGAM1959 host target gene.

TCIRG1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TCIRG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCIRG1 BINDING SITE, designated SEQ ID:12690, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67631] Another function of VGAM1959 is therefore inhibition of T-cell, Immune Regulator 1, ATPase, H<sup>+</sup> Transporting, Lysosomal V0 Protein A Isoform 3 (TCIRG1, Accession NM\_006053), a gene which seems to be directly involved in t cell activation. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCIRG1. The function of TCIRG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1707. Thyroid Hormone Receptor, Alpha (erythroblastic leukemia viral (v-erb-a) Oncogene Homolog, Avian) (THRA, Accession NM\_003250) is another

VGAM1959 host target gene. THRA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by THRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THRA BINDING SITE, designated SEQ ID:9258, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67632] Another function of VGAM1959 is therefore inhibition of Thyroid Hormone Receptor, Alpha (erythroblastic leukemia viral (v-erb-a) Oncogene Homolog, Avian) (THRA, Accession NM\_003250), a gene which is a high affinity receptor for thyroid hormone. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THRA. The function of THRA has been established by previous studies. Debuire et al. (1984) found that ERBA, which potentiates ERBB (OMIM Ref. No. 131550), has an amino acid sequence different from that of other known oncogene products and related to those of the carbonic anhydrases. ERBA potentiates ERBB by blocking differentiation of erythroblasts at an immature stage. Carbonic anhydrases

participate in the transport of carbon dioxide in erythrocytes. Sap et al. (1986) and Weinberger et al. (1986) showed that the ERBA protein is a high-affinity receptor for thyroid hormone. The cDNA sequence indicates a relationship to steroid-hormone receptors, and binding studies indicate that it is a receptor for thyroid hormones. It is located in the nucleus, where it binds to DNA and activates transcription. McCabe et al. (1999) hypothesized that aberrant THRA expression in nonfunctioning pituitary tumors may reflect mutations in the receptor coding and regulatory sequences. They screened THRA mRNA and THRB response elements and ligand-binding domains for sequence anomalies. Screening THRA mRNA from 23 tumors by RNase mismatch and sequencing candidate fragments identified 1 silent and 3 missense mutations, 2 in the common THRA region (190120.0001, 190120.0002) and 1 that was specific for the alpha-2 isoform (190120.0003). No THRB response element differences were detected in 14 nonfunctioning tumors, and no THRB ligand-binding domain differences were detected in 23 nonfunctioning tumors. The authors suggested that the novel thyroid receptor mutations may be of functional significance in terms of thyroid receptor action, and fur-

ther definition of their functional properties may provide insight into the role of thyroid receptors in growth control in pituitary cells. Animal model experiments lend further support to the function of THRA. To evaluate the respective contributions of THRA and THRB in the regulation of CYP7A (OMIM Ref. No. 118455), the rate-limiting enzyme in the synthesis of bile acids, Gullberg et al. (2000) studied the responses to 2% dietary cholesterol and T3 in THRA and THRB knockout mice under hypo- and hyperthyroid conditions. Their experiments showed that the normal stimulation in CYP7A activity and mRNA level by T3 is lost in THRB  $-/-$ , but not in THRA  $-/-$ , mice, identifying THRB as the mediator of T3 action on CYP7A and, consequently, as a major regulator of cholesterol metabolism in vivo. Somewhat unexpectedly, T3-deficient THRB  $-/-$  mice showed an augmented CYP7A response after challenge with dietary cholesterol, and these animals did not develop hypercholesterolemia to the extent that wildtype controls did. The authors concluded that the latter results lend strong support to the concept that THRs may exert regulatory effects in vivo independent of T3.

[67633] It is appreciated that the abovementioned animal model for THRA is acknowledged by those skilled in the art as a

scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[67634] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67635] Weinberger, C.; Thompson, C. C.; Ong, E. S.; Lebo, R.; Gruol, D. J.; Evans, R. M. : The c-erb-A gene encodes a thyroid hormone receptor. Nature 324: 641–646, 1986. ; and

[67636] Gullberg, H.; Rudling, M.; Forrest, D.; Angelin, B.; Vennstrom, B. : Thyroid hormone receptor beta-deficient mice show complete loss of the normal cholesterol 7-alpha-hydroxylase (CYP7A).

[67637] Further studies establishing the function and utilities of THRA are found in John Hopkins OMIM database record ID 190120, and in sited publications numbered 11591–9823, 10340, 1074 and 10569–10571 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TIC (Accession NM\_012455) is another VGAM1959 host target gene. TIC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TIC, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIC BINDING SITE, designated SEQ ID:14830, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67638] Another function of VGAM1959 is therefore inhibition of TIC (Accession NM\_012455). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIC. TIM3 (Accession NM\_032782) is another VGAM1959 host target gene. TIM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIM3 BINDING SITE, designated SEQ ID:26526, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67639] Another function of VGAM1959 is therefore inhibition of TIM3 (Accession NM\_032782), a gene which regulates macrophage activation and enhances the severity of experimental autoimmune encephalomyelitis in mice. Ac-

cordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIM3. The function of TIM3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM909. Translocase of Outer Mitochondrial Membrane 22 Homolog (yeast) (TOMM22, Accession NM\_020243) is another VGAM1959 host target gene. TOMM22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOMM22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOMM22 BINDING SITE, designated SEQ ID:21517, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67640] Another function of VGAM1959 is therefore inhibition of Translocase of Outer Mitochondrial Membrane 22 Homolog (yeast) (TOMM22, Accession NM\_020243). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOMM22. Topoisomerase (DNA) III Beta (TOP3B,



Accession NM\_003935) is another VGAM1959 host target gene. TOP3B BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TOP3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOP3B BINDING SITE, designated SEQ ID:10039, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67641] Another function of VGAM1959 is therefore inhibition of Topoisomerase (DNA) III Beta (TOP3B, Accession NM\_003935). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOP3B. Tripartite Motif-containing 9 (TRIM9, Accession NM\_015163) is another VGAM1959 host target gene. TRIM9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIM9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM9 BINDING SITE, designated SEQ ID:17520, to the nucleotide sequence of

VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67642] Another function of VGAM1959 is therefore inhibition of Tripartite Motif-containing 9 (TRIM9, Accession NM\_015163), a gene which may function as a positive regulator for mannosylphosphate transferase and is required to mediate mannosylphosphate transfer in both the core and outer chain portions of n-linked oligosaccharides. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM9. The function of TRIM9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM\_017662) is another VGAM1959 host target gene. TRPM6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM6 BINDING SITE, designated SEQ ID:19199, to the nucleotide sequence of

VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67643] Another function of VGAM1959 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM\_017662), a gene which contains a predicted ion channel domain and a protein kinase domain. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM6. The function of TRPM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173. Ubiquitin-conjugating Enzyme E2L 3 (UBE2L3, Accession NM\_003347) is another VGAM1959 host target gene. UBE2L3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2L3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2L3 BINDING SITE, designated SEQ ID:9358, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67644] Another function of VGAM1959 is therefore inhibition of Ubiquitin–conjugating Enzyme E2L 3 (UBE2L3, Accession NM\_003347), a gene which catalyzes the covalent attachment of ubiquitin to other proteins. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2L3. The function of UBE2L3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM215. Ubiquitin–conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM\_003349) is another VGAM1959 host target gene. UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UBE2V1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE6, designated SEQ ID:9370, SEQ ID:9372, SEQ ID:22769, SEQ ID:22771, SEQ ID:22522 and SEQ ID:22524 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67645] Another function of VGAM1959 is therefore inhibition of Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM\_003349), a gene which may play a role in signaling for DNA repair. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2V1. The function of UBE2V1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM155. Ubiquitin Specific Protease 11 (USP11, Accession NM\_004651) is another VGAM1959 host target gene. USP11 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by USP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP11 BINDING SITE, designated SEQ ID:11020, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67646] Another function of VGAM1959 is therefore inhibition of Ubiquitin Specific Protease 11 (USP11, Accession NM\_004651), a gene which removes ubiquitin from ubiq-

uitin-conjugated proteins. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP11. The function of USP11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM429. Vang-like 2 (van gogh, Drosophila) (VANGL2, Accession XM\_049695) is another VGAM1959 host target gene. VANGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VANGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VANGL2 BINDING SITE, designated SEQ ID:35478, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67647] Another function of VGAM1959 is therefore inhibition of Vang-like 2 (van gogh, Drosophila) (VANGL2, Accession XM\_049695), a gene which may take part in defining the lateral boundary of floorplate differentiation. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with VANGL2. The function of VANGL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM111. Vasoactive Intestinal Peptide Receptor 2 (VIPR2, Accession NM\_003382) is another VGAM1959 host target gene. VIPR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VIPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VIPR2 BINDING SITE, designated SEQ ID:9413, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67648] Another function of VGAM1959 is therefore inhibition of Vasoactive Intestinal Peptide Receptor 2 (VIPR2, Accession NM\_003382). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIPR2. Very Low Density Lipoprotein Receptor (VLDLR, Accession XM\_045386) is another VGAM1959 host target gene. VLDLR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VLDLR, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VLDLR BINDING SITE, designated SEQ ID:34451, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67649] Another function of VGAM1959 is therefore inhibition of Very Low Density Lipoprotein Receptor (VLDLR, Accession XM\_045386), a gene which may play a crucial role in triglyceride metabolism. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VLDLR. The function of VLDLR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM103.WWP2 (Accession XM\_028151) is another VGAM1959 host target gene. WWP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WWP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WWP2 BINDING SITE, designated SEQ ID:30623, to the nucleotide sequence of



VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67650] Another function of VGAM1959 is therefore inhibition of WWP2 (Accession XM\_028151), a gene which exhibits ubiquitin-protein ligase activity and contains WW and HECT domains. Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WWP2. The function of WWP2 has been established by previous studies. The WW domain is a protein motif consisting of 35 to 40 amino acids and is characterized by 4 conserved aromatic residues, 2 of which are tryptophan. Pirozzi et al. (1997) suggested that WW domains mediate specific protein-protein interactions. Pirozzi et al. (1997) identified WWP2 by screening for WW-domain containing proteins (see OMIM Ref. No. WWP1; 602307). WWP2 contains 4 tandem WW domains, a complete HECT (homologous to the E6-associated protein carboxyl terminus) domain, associated with ubiquitin-protein ligase activity, and a C2 (calcium-dependent phospholipid-binding)-like domain characteristic of a large family of proteins including protein kinase C (see OMIM Ref. No. 176960). Based on similarities in structure between NEDD4 (OMIM Ref. No.

602278) and WWP2, Pirozzi et al. (1997) suggested that WWP2 belongs to a family of NEDD4-like proteins. Using in vitro assays, Pirozzi et al. (1997) showed that individual WW domains can selectively bind particular peptide ligands. By Northern blot analysis, Wood et al. (1998) detected a 5-kb WWP2 transcript in heart, brain, placenta, lung, liver, muscle, kidney, pancreas. Using yeast 2-hybrid and in vitro binding studies, Wood et al. (1998) demonstrated that WWP2, which they called AIP2, binds to atrophin-1 (DRPLA; 125370).

[67651] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[67652] Pirozzi, G.; McConnell, S. J.; Uveges, A. J.; Carter, J. M.; Sparks, A. B.; Kay, B. K.; Fowlkes, D. M. : Identification of novel human WW domain-containing proteins by cloning of ligand targets. *J. Biol. Chem.* 272: 14611-14616, 1997.  
; and

[67653] Wood, J. D.; Yuan, J.; Margolis, R. L.; Colomer, V.; Duan, K.; Kushi, J.; Kaminsky, Z.; Kleiderlein, J. J., Jr.; Sharp, A. H.; Ross, C. A. : Atrophin-1, the DRPLA gene product, interacts.

[67654] Further studies establishing the function and utilities of

WWP2 are found in John Hopkins OMIM database record ID 602308, and in cited publications numbered 5898 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 132 (clone pHZ-12) (ZNF132, Accession NM\_003433) is another VGAM1959 host target gene. ZNF132 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF132 BINDING SITE, designated SEQ ID:9485, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67655] Another function of VGAM1959 is therefore inhibition of Zinc Finger Protein 132 (clone pHZ-12) (ZNF132, Accession NM\_003433). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF132. Zinc Finger Protein 24 (KOX 17) (ZNF24, Accession NM\_006965) is another VGAM1959 host target gene. ZNF24 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF24, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF24 BINDING SITE, designated SEQ ID:13839, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67656] Another function of VGAM1959 is therefore inhibition of Zinc Finger Protein 24 (KOX 17) (ZNF24, Accession NM\_006965). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF24. Zinc Finger Protein 266 (ZNF266, Accession XM\_113992) is another VGAM1959 host target gene. ZNF266 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF266 BINDING SITE, designated SEQ ID:42601, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67657] Another function of VGAM1959 is therefore inhibition of Zinc Finger Protein 266 (ZNF266, Accession XM\_113992).

Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF266. Zinc Finger Protein 268 (ZNF268, Accession XM\_031851) is another VGAM1959 host target gene. ZNF268 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF268 BINDING SITE, designated SEQ ID:31502, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67658] Another function of VGAM1959 is therefore inhibition of Zinc Finger Protein 268 (ZNF268, Accession XM\_031851). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF268. Zinc Finger Protein 35 (clone HF.10) (ZNF35, Accession NM\_003420) is another VGAM1959 host target gene. ZNF35 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF35, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF35 BINDING SITE, designated SEQ ID:9464, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67659] Another function of VGAM1959 is therefore inhibition of Zinc Finger Protein 35 (clone HF.10) (ZNF35, Accession NM\_003420). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF35. Alpha 1,4-galactosyltransferase (A4GALT, Accession NM\_017436) is another VGAM1959 host target gene. A4GALT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by A4GALT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of A4GALT BINDING SITE, designated SEQ ID:18895, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67660] Another function of VGAM1959 is therefore inhibition of Alpha 1,4-galactosyltransferase (A4GALT, Accession

NM\_017436). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with A4GALT. Acetyl-Coenzyme A Synthetase 2 (ADP forming) (ACAS2, Accession NM\_139274) is another VGAM1959 host target gene. ACAS2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ACAS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACAS2 BINDING SITE, designated SEQ ID:29265, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67661] Another function of VGAM1959 is therefore inhibition of Acetyl-Coenzyme A Synthetase 2 (ADP forming) (ACAS2, Accession NM\_139274). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACAS2. ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Accession XM\_031949) is another VGAM1959 host target gene. ACTR1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by ACTR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACTR1A BINDING SITE, designated SEQ ID:31534, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67662] Another function of VGAM1959 is therefore inhibition of ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Accession XM\_031949). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACTR1A. AF053356\_CDS3 (Accession NM\_023948) is another VGAM1959 host target gene. AF053356\_CDS3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AF053356\_CDS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AF053356\_CDS3 BINDING SITE, designated SEQ ID:23428, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.



[67663] Another function of VGAM1959 is therefore inhibition of AF053356\_CDS3 (Accession NM\_023948). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AF053356\_CDS3. A Kinase (PRKA) Anchor Protein 7 (AKAP7, Accession NM\_004842) is another VGAM1959 host target gene. AKAP7 BINDING SITE1 through AKAP7 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AKAP7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP7 BINDING SITE1 through AKAP7 BINDING SITE3, designated SEQ ID:11254, SEQ ID:28907 and SEQ ID:18517 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67664] Another function of VGAM1959 is therefore inhibition of A Kinase (PRKA) Anchor Protein 7 (AKAP7, Accession NM\_004842). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP7. Adaptor-related Protein Complex 3, Delta 1 Subunit (AP3D1, Accession

NM\_003938) is another VGAM1959 host target gene.

AP3D1 BINDING SITE1 and AP3D1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AP3D1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP3D1 BINDING SITE1 and AP3D1 BINDING SITE2, designated SEQ ID:10045 and SEQ ID:10050 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67665] Another function of VGAM1959 is therefore inhibition of Adaptor-related Protein Complex 3, Delta 1 Subunit (AP3D1, Accession NM\_003938). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP3D1. Apoptosis Inhibitor 5 (API5, Accession NM\_006595) is another VGAM1959 host target gene. API5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by API5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of API5 BINDING

SITE, designated SEQ ID:13360, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67666] Another function of VGAM1959 is therefore inhibition of Apoptosis Inhibitor 5 (API5, Accession NM\_006595). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with API5. APOARGC (Accession NM\_024492) is another VGAM1959 host target gene. APOARGC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOARGC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOARGC BINDING SITE, designated SEQ ID:23690, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67667] Another function of VGAM1959 is therefore inhibition of APOARGC (Accession NM\_024492). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOARGC. Apolipoprotein L, 3 (APOL3, Accession NM\_014349) is another VGAM1959 host target gene.

APOL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL3 BINDING SITE, designated SEQ ID:15675, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67668] Another function of VGAM1959 is therefore inhibition of Apolipoprotein L, 3 (APOL3, Accession NM\_014349). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL3. ASAH (Accession NM\_004315) is another VGAM1959 host target gene. ASAH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ASAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASAH BINDING SITE, designated SEQ ID:10517, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67669] Another function of VGAM1959 is therefore inhibition of ASAH (Accession NM\_004315). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASAH. ATIP1 (Accession NM\_020749) is another VGAM1959 host target gene. ATIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATIP1 BINDING SITE, designated SEQ ID:21863, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67670] Another function of VGAM1959 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577) is another VGAM1959 host target gene. ATP9A BINDING SITE1 and ATP9A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ATP9A, corresponding to HOST TARGET binding sites

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE1 and ATP9A BINDING SITE2, designated SEQ ID:31083 and SEQ ID:31089 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67671] Another function of VGAM1959 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM\_030577). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. Burkitt Lymphoma Receptor 1, GTP Binding Protein (chemokine (C-X-C motif) Receptor 5) (BLR1, Accession NM\_032966) is another VGAM1959 host target gene. BLR1 BINDING SITE1 and BLR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BLR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLR1 BINDING SITE1 and BLR1 BINDING SITE2, designated SEQ ID:26778 and SEQ ID:7448 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also

designated SEQ ID:4670.

[67672] Another function of VGAM1959 is therefore inhibition of Burkitt Lymphoma Receptor 1, GTP Binding Protein (chemokine (C-X-C motif) Receptor 5) (BLR1, Accession NM\_032966). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLR1. Chromosome 11 Open Reading Frame 11 (C11orf11, Accession XM\_167769) is another VGAM1959 host target gene. C11orf11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C11orf11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf11 BINDING SITE, designated SEQ ID:44786, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67673] Another function of VGAM1959 is therefore inhibition of Chromosome 11 Open Reading Frame 11 (C11orf11, Accession XM\_167769). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf11. Chro-

mosome 15 Open Reading Frame 5 (C15orf5, Accession NM\_030944) is another VGAM1959 host target gene. C15orf5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C15orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C15orf5 BINDING SITE, designated SEQ ID:25216, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67674] Another function of VGAM1959 is therefore inhibition of Chromosome 15 Open Reading Frame 5 (C15orf5, Accession NM\_030944). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C15orf5. Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM\_012072) is another VGAM1959 host target gene. C1QR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1QR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide



sequences of C1QR1 BINDING SITE, designated SEQ ID:14339, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67675] Another function of VGAM1959 is therefore inhibition of Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM\_012072). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QR1. Chromosome 20 Open Reading Frame 100 (C20orf100, Accession NM\_032883) is another VGAM1959 host target gene. C20orf100 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf100 BINDING SITE, designated SEQ ID:26705, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67676] Another function of VGAM1959 is therefore inhibition of Chromosome 20 Open Reading Frame 100 (C20orf100, Accession NM\_032883). Accordingly, utilities of

VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf100. Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM\_080821) is another VGAM1959 host target gene. C20orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf108 BINDING SITE, designated SEQ ID:28084, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67677] Another function of VGAM1959 is therefore inhibition of Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM\_080821). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf108. Chromosome 20 Open Reading Frame 162 (C20orf162, Accession NM\_080603) is another VGAM1959 host target gene. C20orf162 BINDING SITE1 and C20orf162 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

C20orf162, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf162 BINDING SITE1 and C20orf162 BINDING SITE2, designated SEQ ID:27915 and SEQ ID:27918 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67678] Another function of VGAM1959 is therefore inhibition of Chromosome 20 Open Reading Frame 162 (C20orf162, Accession NM\_080603). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf162. Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM\_114191) is another VGAM1959 host target gene. C21orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf108 BINDING SITE, designated SEQ ID:42768, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA,

also designated SEQ ID:4670.

[67679] Another function of VGAM1959 is therefore inhibition of Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM\_114191). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf108. Chromosome 5 Open Reading Frame 5 (C5orf5, Accession NM\_016603) is another VGAM1959 host target gene. C5orf5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C5orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf5 BINDING SITE, designated SEQ ID:18696, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67680] Another function of VGAM1959 is therefore inhibition of Chromosome 5 Open Reading Frame 5 (C5orf5, Accession NM\_016603). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf5. Calcium Channel, Voltage-dependent, Gamma Subunit 4 (CACNG4, Acces-

sion NM\_014405) is another VGAM1959 host target gene. CACNG4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CACNG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNG4 BINDING SITE, designated SEQ ID:15747, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67681] Another function of VGAM1959 is therefore inhibition of Calcium Channel, Voltage-dependent, Gamma Subunit 4 (CACNG4, Accession NM\_014405). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNG4. CAT56 (Accession NM\_025263) is another VGAM1959 host target gene. CAT56 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CAT56, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAT56 BINDING SITE, designated SEQ ID:24932, to the nucleotide sequence of

VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67682] Another function of VGAM1959 is therefore inhibition of CAT56 (Accession NM\_025263). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAT56. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM\_033332) is another VGAM1959 host target gene. CDC14B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC14B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE, designated SEQ ID:27169, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67683] Another function of VGAM1959 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM\_033332). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. Chorionic Gonadotropin, Beta Polypeptide 5

(CGB5, Accession NM\_033043) is another VGAM1959 host target gene. CGB5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CGB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGB5 BINDING SITE, designated SEQ ID:26931, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67684] Another function of VGAM1959 is therefore inhibition of Chorionic Gonadotropin, Beta Polypeptide 5 (CGB5, Accession NM\_033043). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGB5. Chorionic Gonadotropin, Beta Polypeptide 8 (CGB8, Accession NM\_033183) is another VGAM1959 host target gene. CGB8 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CGB8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGB8 BINDING SITE, designated SEQ ID:27046,

to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67685] Another function of VGAM1959 is therefore inhibition of Chorionic Gonadotropin, Beta Polypeptide 8 (CGB8, Accession NM\_033183). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGB8. Calcium Homeostasis Endoplasmic Reticulum Protein (CHERP, Accession NM\_006387) is another VGAM1959 host target gene. CHERP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHERP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHERP BINDING SITE, designated SEQ ID:13093, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67686] Another function of VGAM1959 is therefore inhibition of Calcium Homeostasis Endoplasmic Reticulum Protein (CHERP, Accession NM\_006387). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHERP.



CSE-C (Accession XM\_166163) is another VGAM1959 host target gene. CSE-C BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CSE-C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSE-C BINDING SITE, designated SEQ ID:43981, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67687] Another function of VGAM1959 is therefore inhibition of CSE-C (Accession XM\_166163). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSE-C. Calsenilin, Presenilin Binding Protein, EF Hand Transcription Factor (CSEN, Accession NM\_013434) is another VGAM1959 host target gene. CSEN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CSEN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSEN BINDING SITE, designated SEQ ID:15090, to the nucleotide sequence of

VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67688] Another function of VGAM1959 is therefore inhibition of Calsenilin, Presenilin Binding Protein, EF Hand Transcription Factor (CSEN, Accession NM\_013434). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSEN. Catenin, Beta Interacting Protein 1 (CTNNBIP1, Accession NM\_020248) is another VGAM1959 host target gene. CTNNBIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTNNBIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTNNBIP1 BINDING SITE, designated SEQ ID:21543, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67689] Another function of VGAM1959 is therefore inhibition of Catenin, Beta Interacting Protein 1 (CTNNBIP1, Accession NM\_020248). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTNNBIP1. CXYorf1

(Accession XM\_088704) is another VGAM1959 host target gene. CXYorf1 BINDING SITE1 and CXYorf1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CXYorf1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXYorf1 BINDING SITE1 and CXYorf1 BINDING SITE2, designated SEQ ID:39906 and SEQ ID:39913 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67690] Another function of VGAM1959 is therefore inhibition of CXYorf1 (Accession XM\_088704). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXYorf1. Death-associated Protein Kinase 3 (DAPK3, Accession NM\_001348) is another VGAM1959 host target gene. DAPK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAPK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAPK3 BINDING SITE, designated SEQ

ID:7029, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67691] Another function of VGAM1959 is therefore inhibition of Death-associated Protein Kinase 3 (DAPK3, Accession NM\_001348). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAPK3. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681) is another VGAM1959 host target gene. DDX34 BINDING SITE1 and DDX34 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DDX34, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE1 and DDX34 BINDING SITE2, designated SEQ ID:16160 and SEQ ID:16166 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67692] Another function of VGAM1959 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM\_014681). Accordingly, utilities of

VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. DKFZP434B195 (Accession NM\_031284) is another VGAM1959 host target gene. DKFZP434B195 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434B195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434B195 BINDING SITE, designated SEQ ID:25308, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67693] Another function of VGAM1959 is therefore inhibition of DKFZP434B195 (Accession NM\_031284). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434B195. DKFZp434C0923 (Accession NM\_017598) is another VGAM1959 host target gene. DKFZp434C0923 BINDING SITE1 and DKFZp434C0923 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZp434C0923, corresponding to HOST TARGET binding sites such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434C0923 BINDING SITE1 and DKFZp434C0923 BINDING SITE2, designated SEQ ID:19064 and SEQ ID:19067 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67694] Another function of VGAM1959 is therefore inhibition of DKFZp434C0923 (Accession NM\_017598). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434C0923. DKFZP434C212 (Accession XM\_044196) is another VGAM1959 host target gene. DKFZP434C212 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434C212, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C212 BINDING SITE, designated SEQ ID:34169, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67695] Another function of VGAM1959 is therefore inhibition of

DKFZP434C212 (Accession XM\_044196). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C212. DKFZP434I092 (Accession XM\_042042) is another VGAM1959 host target gene. DKFZP434I092 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434I092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I092 BINDING SITE, designated SEQ ID:33676, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67696] Another function of VGAM1959 is therefore inhibition of DKFZP434I092 (Accession XM\_042042). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I092. DKFZP434I2117 (Accession NM\_031478) is another VGAM1959 host target gene. DKFZP434I2117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434I2117, corresponding to a HOST TARGET bind-

ing site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I2117 BINDING SITE, designated SEQ ID:25555, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67697] Another function of VGAM1959 is therefore inhibition of DKFZP434I2117 (Accession NM\_031478). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I2117. DKFZP434K1772 (Accession XM\_041936) is another VGAM1959 host target gene. DKFZP434K1772 BINDING SITE1 and DKFZP434K1772 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZP434K1772, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434K1772 BINDING SITE1 and DKFZP434K1772 BINDING SITE2, designated SEQ ID:33631 and SEQ ID:33634 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.



[67698] Another function of VGAM1959 is therefore inhibition of DKFZP434K1772 (Accession XM\_041936). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434K1772. DKFZp434N2435 (Accession XM\_172806) is another VGAM1959 host target gene. DKFZp434N2435 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp434N2435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434N2435 BINDING SITE, designated SEQ ID:46090, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67699] Another function of VGAM1959 is therefore inhibition of DKFZp434N2435 (Accession XM\_172806). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434N2435. DKFZp434O0320 (Accession XM\_097012) is another VGAM1959 host target gene. DKFZp434O0320 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

DKFZp434O0320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434O0320 BINDING SITE, designated SEQ ID:40703, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67700] Another function of VGAM1959 is therefore inhibition of DKFZp434O0320 (Accession XM\_097012). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434O0320. DKFZP434O047 (Accession NM\_015594) is another VGAM1959 host target gene. DKFZP434O047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434O047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434O047 BINDING SITE, designated SEQ ID:17866, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67701] Another function of VGAM1959 is therefore inhibition of

DKFZP434O047 (Accession NM\_015594). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434O047. DKFZP434P1750 (Accession NM\_015527) is another VGAM1959 host target gene. DKFZP434P1750 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P1750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P1750 BINDING SITE, designated SEQ ID:17795, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67702] Another function of VGAM1959 is therefore inhibition of DKFZP434P1750 (Accession NM\_015527). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P1750. DKFZP564F013 (Accession XM\_168479) is another VGAM1959 host target gene. DKFZP564F013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564F013, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564F013 BINDING SITE, designated SEQ ID:45201, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67703] Another function of VGAM1959 is therefore inhibition of DKFZP564F013 (Accession XM\_168479). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564F013. DKFZP564J157 (Accession NM\_018457) is another VGAM1959 host target gene. DKFZP564J157 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564J157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564J157 BINDING SITE, designated SEQ ID:20529, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67704] Another function of VGAM1959 is therefore inhibition of DKFZP564J157 (Accession NM\_018457). Accordingly, util-

ities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564J157. DKFZP564P1916 (Accession NM\_015652) is another VGAM1959 host target gene. DKFZP564P1916 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP564P1916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564P1916 BINDING SITE, designated SEQ ID:17899, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67705] Another function of VGAM1959 is therefore inhibition of DKFZP564P1916 (Accession NM\_015652). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564P1916. DKFZp566H0824 (Accession NM\_017535) is another VGAM1959 host target gene. DKFZp566H0824 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp566H0824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp566H0824 BINDING SITE, designated SEQ ID:18978, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67706] Another function of VGAM1959 is therefore inhibition of DKFZp566H0824 (Accession NM\_017535). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp566H0824. DKFZp586I021 (Accession NM\_032271) is another VGAM1959 host target gene. DKFZp586I021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp586I021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586I021 BINDING SITE, designated SEQ ID:26024, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67707] Another function of VGAM1959 is therefore inhibition of DKFZp586I021 (Accession NM\_032271). Accordingly, utilities of VGAM1959 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZp586I021. DKFZP586M1120 (Accession NM\_031294) is another VGAM1959 host target gene. DKFZP586M1120 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586M1120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586M1120 BINDING SITE, designated SEQ ID:25320, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67708] Another function of VGAM1959 is therefore inhibition of DKFZP586M1120 (Accession NM\_031294). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586M1120. DKFZP761D0211 (Accession NM\_032039) is another VGAM1959 host target gene. DKFZP761D0211 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP761D0211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of DKFZP761D0211 BINDING SITE, designated SEQ ID:25738, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67709] Another function of VGAM1959 is therefore inhibition of DKFZP761D0211 (Accession NM\_032039). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761D0211. DKFZp762M136 (Accession XM\_035635) is another VGAM1959 host target gene. DKFZp762M136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762M136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762M136 BINDING SITE, designated SEQ ID:32303, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67710] Another function of VGAM1959 is therefore inhibition of DKFZp762M136 (Accession XM\_035635). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated



with DKFZp762M136. DKFZp762P2111 (Accession XM\_098654) is another VGAM1959 host target gene. DKFZp762P2111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762P2111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762P2111 BINDING SITE, designated SEQ ID:41756, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67711] Another function of VGAM1959 is therefore inhibition of DKFZp762P2111 (Accession XM\_098654). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762P2111. Dihydrolipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex) (DLAT, Accession XM\_041355) is another VGAM1959 host target gene. DLAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DLAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of DLAT BINDING SITE, designated SEQ ID:33502, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67712] Another function of VGAM1959 is therefore inhibition of Dihydrolipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex) (DLAT, Accession XM\_041355). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLAT. DRIL2 (Accession NM\_006465) is another VGAM1959 host target gene. DRIL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DRIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRIL2 BINDING SITE, designated SEQ ID:13187, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67713] Another function of VGAM1959 is therefore inhibition of DRIL2 (Accession NM\_006465). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRIL2.

DT1P1A10 (Accession XM\_029187) is another VGAM1959 host target gene. DT1P1A10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DT1P1A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DT1P1A10 BINDING SITE, designated SEQ ID:30860, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67714] Another function of VGAM1959 is therefore inhibition of DT1P1A10 (Accession XM\_029187). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DT1P1A10. DVS27 (Accession NM\_033439) is another VGAM1959 host target gene. DVS27 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DVS27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVS27 BINDING SITE, designated SEQ ID:27251, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4670.

[67715] Another function of VGAM1959 is therefore inhibition of DVS27 (Accession NM\_033439). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVS27. Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295) is another VGAM1959 host target gene. EPB41L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPB41L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L1 BINDING SITE, designated SEQ ID:34940, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67716] Another function of VGAM1959 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM\_047295). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L1. F-box Only Protein 27 (FBXO27, Accession XM\_059045) is another VGAM1959 host target gene.

FBXO27 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO27 BINDING SITE, designated SEQ ID:36835, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67717] Another function of VGAM1959 is therefore inhibition of F-box Only Protein 27 (FBXO27, Accession XM\_059045). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO27. FK506 Binding Protein 14, 22 KDa (FKBP14, Accession NM\_017946) is another VGAM1959 host target gene. FKBP14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FKBP14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKBP14 BINDING SITE, designated SEQ ID:19644, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA,

also designated SEQ ID:4670.

[67718] Another function of VGAM1959 is therefore inhibition of FK506 Binding Protein 14, 22 KDa (FKBP14, Accession NM\_017946). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKBP14. FK506 Binding Protein 5 (FKBP5, Accession NM\_004117) is another VGAM1959 host target gene. FKBP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FKBP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKBP5 BINDING SITE, designated SEQ ID:10325, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67719] Another function of VGAM1959 is therefore inhibition of FK506 Binding Protein 5 (FKBP5, Accession NM\_004117). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKBP5. FK506 Binding Protein 9, 63 KDa (FKBP9, Accession XM\_168403) is another VGAM1959 host target gene. FKBP9 BINDING SITE is HOST TARGET

binding site found in the 5` untranslated region of mRNA encoded by FKBP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKBP9 BINDING SITE, designated SEQ ID:45145, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67720] Another function of VGAM1959 is therefore inhibition of FK506 Binding Protein 9, 63 KDa (FKBP9, Accession XM\_168403). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKBP9. FKSG28 (Accession NM\_030929) is another VGAM1959 host target gene. FKSG28 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FKSG28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKSG28 BINDING SITE, designated SEQ ID:25203, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67721] Another function of VGAM1959 is therefore inhibition of FKSG28 (Accession NM\_030929). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKSG28. FLJ00026 (Accession XM\_036307) is another VGAM1959 host target gene. FLJ00026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00026 BINDING SITE, designated SEQ ID:32426, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67722] Another function of VGAM1959 is therefore inhibition of FLJ00026 (Accession XM\_036307). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00026. FLJ00060 (Accession XM\_028154) is another VGAM1959 host target gene. FLJ00060 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ00060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00060 BINDING SITE, designated SEQ ID:30629, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67723] Another function of VGAM1959 is therefore inhibition of FLJ00060 (Accession XM\_028154). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00060. FLJ10159 (Accession NM\_018013) is another VGAM1959 host target gene. FLJ10159 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10159 BINDING SITE, designated SEQ ID:19750, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67724] Another function of VGAM1959 is therefore inhibition of FLJ10159 (Accession NM\_018013). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10159. FLJ10656 (Accession NM\_018170) is another VGAM1959 host target gene. FLJ10656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10656 BINDING SITE, designated SEQ ID:19990, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67725] Another function of VGAM1959 is therefore inhibition of FLJ10656 (Accession NM\_018170). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10656. FLJ10724 (Accession NM\_018194) is another VGAM1959 host target gene. FLJ10724 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10724, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10724 BINDING SITE, designated SEQ ID:20050, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM

RNA, also designated SEQ ID:4670.

[67726] Another function of VGAM1959 is therefore inhibition of FLJ10724 (Accession NM\_018194). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10724. FLJ10737 (Accession NM\_018198) is another VGAM1959 host target gene. FLJ10737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10737 BINDING SITE, designated SEQ ID:20066, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67727] Another function of VGAM1959 is therefore inhibition of FLJ10737 (Accession NM\_018198). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10737. FLJ10803 (Accession NM\_018224) is another VGAM1959 host target gene. FLJ10803 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10803, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10803 BINDING SITE, designated SEQ ID:20151, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67728] Another function of VGAM1959 is therefore inhibition of FLJ10803 (Accession NM\_018224). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10803. FLJ11252 (Accession XM\_041702) is another VGAM1959 host target gene. FLJ11252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11252 BINDING SITE, designated SEQ ID:33567, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67729] Another function of VGAM1959 is therefore inhibition of FLJ11252 (Accession XM\_041702). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ11252. FLJ11710 (Accession NM\_024846) is another VGAM1959 host target gene. FLJ11710 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11710, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11710 BINDING SITE, designated SEQ ID:24274, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67730] Another function of VGAM1959 is therefore inhibition of FLJ11710 (Accession NM\_024846). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11710. FLJ12122 (Accession NM\_024979) is another VGAM1959 host target gene. FLJ12122 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12122 BINDING SITE, designated SEQ ID:24539, to the nucleotide

sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67731] Another function of VGAM1959 is therefore inhibition of FLJ12122 (Accession NM\_024979). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12122. FLJ12190 (Accession NM\_025071) is another VGAM1959 host target gene. FLJ12190 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12190 BINDING SITE, designated SEQ ID:24668, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67732] Another function of VGAM1959 is therefore inhibition of FLJ12190 (Accession NM\_025071). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12190. FLJ12287 (Accession NM\_022367) is another VGAM1959 host target gene. FLJ12287 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by FLJ12287, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12287 BINDING SITE, designated SEQ ID:22754, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67733] Another function of VGAM1959 is therefore inhibition of FLJ12287 (Accession NM\_022367). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12287. FLJ12443 (Accession NM\_024830) is another VGAM1959 host target gene. FLJ12443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12443 BINDING SITE, designated SEQ ID:24223, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67734] Another function of VGAM1959 is therefore inhibition of FLJ12443 (Accession NM\_024830). Accordingly, utilities of

VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12443. FLJ12517 (Accession NM\_023007) is another VGAM1959 host target gene. FLJ12517 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12517, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12517 BINDING SITE, designated SEQ ID:23268, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67735] Another function of VGAM1959 is therefore inhibition of FLJ12517 (Accession NM\_023007). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12517. FLJ12547 (Accession NM\_024992) is another VGAM1959 host target gene. FLJ12547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12547



BINDING SITE, designated SEQ ID:24548, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67736] Another function of VGAM1959 is therefore inhibition of FLJ12547 (Accession NM\_024992). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12547. FLJ12650 (Accession NM\_024522) is another VGAM1959 host target gene. FLJ12650 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12650 BINDING SITE, designated SEQ ID:23724, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67737] Another function of VGAM1959 is therefore inhibition of FLJ12650 (Accession NM\_024522). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12650. FLJ12687 (Accession NM\_024917) is another VGAM1959 host target gene. FLJ12687 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12687 BINDING SITE, designated SEQ ID:24445, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67738] Another function of VGAM1959 is therefore inhibition of FLJ12687 (Accession NM\_024917). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12687. FLJ12800 (Accession NM\_022903) is another VGAM1959 host target gene. FLJ12800 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12800 BINDING SITE, designated SEQ ID:23190, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67739] Another function of VGAM1959 is therefore inhibition of

FLJ12800 (Accession NM\_022903). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12800. FLJ12895 (Accession NM\_023926) is another VGAM1959 host target gene. FLJ12895 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12895 BINDING SITE, designated SEQ ID:23404, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67740] Another function of VGAM1959 is therefore inhibition of FLJ12895 (Accession NM\_023926). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12895. FLJ13072 (Accession XM\_117117) is another VGAM1959 host target gene. FLJ13072 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ13072 BINDING SITE, designated SEQ ID:43239, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67741] Another function of VGAM1959 is therefore inhibition of FLJ13072 (Accession XM\_117117). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13072. FLJ13158 (Accession NM\_024909) is another VGAM1959 host target gene. FLJ13158 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13158 BINDING SITE, designated SEQ ID:24409, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67742] Another function of VGAM1959 is therefore inhibition of FLJ13158 (Accession NM\_024909). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13158. FLJ13181 (Accession NM\_025188) is another

VGAM1959 host target gene. FLJ13181 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13181 BINDING SITE, designated SEQ ID:24828, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67743] Another function of VGAM1959 is therefore inhibition of FLJ13181 (Accession NM\_025188). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13181. FLJ13544 (Accession NM\_025008) is another VGAM1959 host target gene. FLJ13544 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13544, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13544 BINDING SITE, designated SEQ ID:24579, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67744] Another function of VGAM1959 is therefore inhibition of FLJ13544 (Accession NM\_025008). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13544. FLJ13910 (Accession NM\_022780) is another VGAM1959 host target gene. FLJ13910 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13910 BINDING SITE, designated SEQ ID:23056, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67745] Another function of VGAM1959 is therefore inhibition of FLJ13910 (Accession NM\_022780). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13910. FLJ14084 (Accession NM\_021637) is another VGAM1959 host target gene. FLJ14084 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14084 BINDING SITE, designated SEQ ID:22284, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67746] Another function of VGAM1959 is therefore inhibition of FLJ14084 (Accession NM\_021637). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14084. FLJ14213 (Accession NM\_024841) is another VGAM1959 host target gene. FLJ14213 BINDING SITE1 and FLJ14213 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ14213, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14213 BINDING SITE1 and FLJ14213 BINDING SITE2, designated SEQ ID:24256 and SEQ ID:24257 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67747] Another function of VGAM1959 is therefore inhibition of FLJ14213 (Accession NM\_024841). Accordingly, utilities of

VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14213. FLJ14641 (Accession NM\_032817) is another VGAM1959 host target gene. FLJ14641 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14641, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14641 BINDING SITE, designated SEQ ID:26589, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67748] Another function of VGAM1959 is therefore inhibition of FLJ14641 (Accession NM\_032817). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14641. FLJ14681 (Accession NM\_032824) is another VGAM1959 host target gene. FLJ14681 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14681



BINDING SITE, designated SEQ ID:26597, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67749] Another function of VGAM1959 is therefore inhibition of FLJ14681 (Accession NM\_032824). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14681. FLJ14743 (Accession XM\_042708) is another VGAM1959 host target gene. FLJ14743 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14743 BINDING SITE, designated SEQ ID:33764, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67750] Another function of VGAM1959 is therefore inhibition of FLJ14743 (Accession XM\_042708). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14743. FLJ14816 (Accession NM\_032845) is another VGAM1959 host target gene. FLJ14816 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14816, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14816 BINDING SITE, designated SEQ ID:26639, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67751] Another function of VGAM1959 is therefore inhibition of FLJ14816 (Accession NM\_032845). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14816. FLJ14957 (Accession NM\_032866) is another VGAM1959 host target gene. FLJ14957 BINDING SITE1 and FLJ14957 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ14957, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14957 BINDING SITE1 and FLJ14957 BINDING SITE2, designated SEQ ID:26681 and SEQ ID:26684 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4670.

[67752] Another function of VGAM1959 is therefore inhibition of FLJ14957 (Accession NM\_032866). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14957. FLJ20209 (Accession XM\_098142) is another VGAM1959 host target gene. FLJ20209 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20209, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20209 BINDING SITE, designated SEQ ID:41405, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67753] Another function of VGAM1959 is therefore inhibition of FLJ20209 (Accession XM\_098142). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20209. FLJ20297 (Accession NM\_017951) is another VGAM1959 host target gene. FLJ20297 BINDING SITE1 and FLJ20297 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

FLJ20297, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20297 BINDING SITE1 and FLJ20297 BINDING SITE2, designated SEQ ID:19651 and SEQ ID:19360 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67754] Another function of VGAM1959 is therefore inhibition of FLJ20297 (Accession NM\_017951). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20297. FLJ20477 (Accession NM\_017837) is another VGAM1959 host target gene. FLJ20477 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20477 BINDING SITE, designated SEQ ID:19502, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67755] Another function of VGAM1959 is therefore inhibition of

FLJ20477 (Accession NM\_017837). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20477. FLJ20509 (Accession NM\_017851) is another VGAM1959 host target gene. FLJ20509 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20509 BINDING SITE, designated SEQ ID:19523, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67756] Another function of VGAM1959 is therefore inhibition of FLJ20509 (Accession NM\_017851). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20509. FLJ21276 (Accession NM\_024633) is another VGAM1959 host target gene. FLJ21276 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ21276 BINDING SITE, designated SEQ ID:23904, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67757] Another function of VGAM1959 is therefore inhibition of FLJ21276 (Accession NM\_024633). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21276. FLJ21313 (Accession NM\_023927) is another VGAM1959 host target gene. FLJ21313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21313 BINDING SITE, designated SEQ ID:23408, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67758] Another function of VGAM1959 is therefore inhibition of FLJ21313 (Accession NM\_023927). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21313. FLJ21551 (Accession NM\_024801) is another

VGAM1959 host target gene. FLJ21551 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21551, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21551 BINDING SITE, designated SEQ ID:24180, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67759] Another function of VGAM1959 is therefore inhibition of FLJ21551 (Accession NM\_024801). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21551. FLJ21865 (Accession NM\_022759) is another VGAM1959 host target gene. FLJ21865 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21865 BINDING SITE, designated SEQ ID:23000, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67760] Another function of VGAM1959 is therefore inhibition of FLJ21865 (Accession NM\_022759). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21865. FLJ22035 (Accession NM\_024523) is another VGAM1959 host target gene. FLJ22035 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22035, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22035 BINDING SITE, designated SEQ ID:23725, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67761] Another function of VGAM1959 is therefore inhibition of FLJ22035 (Accession NM\_024523). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22035. FLJ22233 (Accession NM\_024959) is another VGAM1959 host target gene. FLJ22233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-



ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22233 BINDING SITE, designated SEQ ID:24515, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67762] Another function of VGAM1959 is therefore inhibition of FLJ22233 (Accession NM\_024959). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22233. FLJ22341 (Accession NM\_024599) is another VGAM1959 host target gene. FLJ22341 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22341, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22341 BINDING SITE, designated SEQ ID:23849, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67763] Another function of VGAM1959 is therefore inhibition of FLJ22341 (Accession NM\_024599). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ22341. FLJ22474 (Accession NM\_024719) is another VGAM1959 host target gene. FLJ22474 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22474, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22474 BINDING SITE, designated SEQ ID:24050, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67764] Another function of VGAM1959 is therefore inhibition of FLJ22474 (Accession NM\_024719). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22474. FLJ22479 (Accession NM\_024900) is another VGAM1959 host target gene. FLJ22479 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22479 BINDING SITE, designated SEQ ID:24387, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM

RNA, also designated SEQ ID:4670.

[67765] Another function of VGAM1959 is therefore inhibition of FLJ22479 (Accession NM\_024900). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22479. FLJ22679 (Accession NM\_032227) is another VGAM1959 host target gene. FLJ22679 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22679, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22679 BINDING SITE, designated SEQ ID:25949, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67766] Another function of VGAM1959 is therefore inhibition of FLJ22679 (Accession NM\_032227). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22679. FLJ22761 (Accession NM\_025130) is another VGAM1959 host target gene. FLJ22761 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22761, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22761 BINDING SITE, designated SEQ ID:24773, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67767] Another function of VGAM1959 is therefore inhibition of FLJ22761 (Accession NM\_025130). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22761. FLJ22940 (Accession NM\_024571) is another VGAM1959 host target gene. FLJ22940 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22940 BINDING SITE, designated SEQ ID:23798, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67768] Another function of VGAM1959 is therefore inhibition of FLJ22940 (Accession NM\_024571). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ22940. FLJ23091 (Accession NM\_024911) is another VGAM1959 host target gene. FLJ23091 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23091 BINDING SITE, designated SEQ ID:24418, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67769] Another function of VGAM1959 is therefore inhibition of FLJ23091 (Accession NM\_024911). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23091. FLJ23309 (Accession NM\_024896) is another VGAM1959 host target gene. FLJ23309 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23309, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23309 BINDING SITE, designated SEQ ID:24380, to the nucleotide

sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67770] Another function of VGAM1959 is therefore inhibition of FLJ23309 (Accession NM\_024896). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23309. FLJ23499 (Accession NM\_022761) is another VGAM1959 host target gene. FLJ23499 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23499 BINDING SITE, designated SEQ ID:23007, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67771] Another function of VGAM1959 is therefore inhibition of FLJ23499 (Accession NM\_022761). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23499. FLJ23556 (Accession NM\_024880) is another VGAM1959 host target gene. FLJ23556 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ23556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23556 BINDING SITE, designated SEQ ID:24320, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67772] Another function of VGAM1959 is therefore inhibition of FLJ23556 (Accession NM\_024880). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23556. FLJ25442 (Accession NM\_145026) is another VGAM1959 host target gene. FLJ25442 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ25442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ25442 BINDING SITE, designated SEQ ID:29641, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67773] Another function of VGAM1959 is therefore inhibition of FLJ25442 (Accession NM\_145026). Accordingly, utilities of

VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ25442. FLJ31709 (Accession NM\_144636) is another VGAM1959 host target gene. FLJ31709 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31709 BINDING SITE, designated SEQ ID:29460, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67774] Another function of VGAM1959 is therefore inhibition of FLJ31709 (Accession NM\_144636). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31709. FLJ31951 (Accession NM\_144726) is another VGAM1959 host target gene. FLJ31951 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31951, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31951



BINDING SITE, designated SEQ ID:29551, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67775] Another function of VGAM1959 is therefore inhibition of FLJ31951 (Accession NM\_144726). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31951. FLJ32334 (Accession NM\_144565) is another VGAM1959 host target gene. FLJ32334 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32334, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32334 BINDING SITE, designated SEQ ID:29369, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67776] Another function of VGAM1959 is therefore inhibition of FLJ32334 (Accession NM\_144565). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32334. Forkhead Box O3A (FOXO3A, Accession NM\_001455) is another VGAM1959 host target gene.

FOXO3A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FOXO3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXO3A BINDING SITE, designated SEQ ID:7190, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67777] Another function of VGAM1959 is therefore inhibition of Forkhead Box O3A (FOXO3A, Accession NM\_001455). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXO3A. Frequentin Homolog (Drosophila) (FREQ, Accession NM\_014286) is another VGAM1959 host target gene. FREQ BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FREQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FREQ BINDING SITE, designated SEQ ID:15564, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ

ID:4670.

[67778] Another function of VGAM1959 is therefore inhibition of Frequentin Homolog (Drosophila) (FREQ, Accession NM\_014286). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FREQ. FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM\_054016) is another VGAM1959 host target gene. FUSIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUSIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUSIP1 BINDING SITE, designated SEQ ID:27625, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67779] Another function of VGAM1959 is therefore inhibition of FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM\_054016). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUSIP1. Glutamine-fructose-6-phosphate Transaminase 1 (GFPT1,

Accession NM\_002056) is another VGAM1959 host target gene. GFPT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFPT1 BINDING SITE, designated SEQ ID:7820, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67780] Another function of VGAM1959 is therefore inhibition of Glutamine-fructose-6-phosphate Transaminase 1 (GFPT1, Accession NM\_002056). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFPT1. Gamma-glutamyltransferase-like Activity 4 (GGTLA4, Accession NM\_080920) is another VGAM1959 host target gene. GGTLA4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GGTLA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGTLA4 BINDING SITE, designated SEQ

ID:28142, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67781] Another function of VGAM1959 is therefore inhibition of Gamma-glutamyltransferase-like Activity 4 (GGTLA4, Accession NM\_080920). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGTLA4. Guanine Nucleotide Binding Protein (G protein), Gamma 11 (GNG11, Accession NM\_004126) is another VGAM1959 host target gene. GNG11 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GNG11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNG11 BINDING SITE, designated SEQ ID:10333, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67782] Another function of VGAM1959 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Gamma 11 (GNG11, Accession NM\_004126). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with GNG11. Glutamic Pyruvate Transaminase (alanine aminotransferase) 2 (GPT2, Accession NM\_133443) is another VGAM1959 host target gene. GPT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPT2 BINDING SITE, designated SEQ ID:28523, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67783] Another function of VGAM1959 is therefore inhibition of Glutamic Pyruvate Transaminase (alanine aminotransferase) 2 (GPT2, Accession NM\_133443). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPT2. GR6 (Accession NM\_007354) is another VGAM1959 host target gene. GR6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GR6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of GR6 BINDING SITE, designated SEQ ID:14282, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67784] Another function of VGAM1959 is therefore inhibition of GR6 (Accession NM\_007354). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GR6. Glutamate Receptor, Ionotropic, N-methyl-D-aspartate 3A (GRIN3A, Accession NM\_133445) is another VGAM1959 host target gene. GRIN3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRIN3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN3A BINDING SITE, designated SEQ ID:28533, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67785] Another function of VGAM1959 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl-D-aspartate 3A (GRIN3A, Accession NM\_133445). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with GRIN3A. GS3955 (Accession NM\_021643) is another VGAM1959 host target gene. GS3955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GS3955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GS3955 BINDING SITE, designated SEQ ID:22306, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67786] Another function of VGAM1959 is therefore inhibition of GS3955 (Accession NM\_021643). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GS3955. General Transcription Factor IIIC, Polypeptide 1, Alpha 220kDa (GTF3C1, Accession NM\_001520) is another VGAM1959 host target gene. GTF3C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GTF3C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTF3C1



BINDING SITE, designated SEQ ID:7260, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67787] Another function of VGAM1959 is therefore inhibition of General Transcription Factor IIIC, Polypeptide 1, Alpha 220kDa (GTF3C1, Accession NM\_001520). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTF3C1. HCCA2 (Accession XM\_039894) is another VGAM1959 host target gene. HCCA2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HCCA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCCA2 BINDING SITE, designated SEQ ID:33203, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67788] Another function of VGAM1959 is therefore inhibition of HCCA2 (Accession XM\_039894). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCCA2. HEMK (Accession NM\_016173) is another VGAM1959 host

target gene. HEMK BINDING SITE1 and HEMK BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HEMK, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEMK BINDING SITE1 and HEMK BINDING SITE2, designated SEQ ID:18267 and SEQ ID:18274 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67789] Another function of VGAM1959 is therefore inhibition of HEMK (Accession NM\_016173). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEMK. HN1L (Accession NM\_144570) is another VGAM1959 host target gene. HN1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HN1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HN1L BINDING SITE, designated SEQ ID:29376, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ

ID:4670.

[67790] Another function of VGAM1959 is therefore inhibition of HN1L (Accession NM\_144570). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HN1L. HPIP (Accession NM\_020524) is another VGAM1959 host target gene. HPIP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HPIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPIP BINDING SITE, designated SEQ ID:21740, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67791] Another function of VGAM1959 is therefore inhibition of HPIP (Accession NM\_020524). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPIP. HRIHFB2122 (Accession NM\_007032) is another VGAM1959 host target gene. HRIHFB2122 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HRIHFB2122, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRI-HFB2122 BINDING SITE, designated SEQ ID:13898, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67792] Another function of VGAM1959 is therefore inhibition of HRIHFB2122 (Accession NM\_007032). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRIHFB2122. HS6ST (Accession XM\_030529) is another VGAM1959 host target gene. HS6ST BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HS6ST, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS6ST BINDING SITE, designated SEQ ID:31073, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67793] Another function of VGAM1959 is therefore inhibition of HS6ST (Accession XM\_030529). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with HS6ST. HSP105B (Accession NM\_006644) is another VGAM1959 host target gene. HSP105B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSP105B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSP105B BINDING SITE, designated SEQ ID:13438, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67794] Another function of VGAM1959 is therefore inhibition of HSP105B (Accession NM\_006644). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSP105B. HT002 (Accession NM\_014066) is another VGAM1959 host target gene. HT002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HT002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HT002 BINDING SITE, designated SEQ ID:15284, to the nucleotide sequence of

VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67795] Another function of VGAM1959 is therefore inhibition of HT002 (Accession NM\_014066). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HT002. HU-K4 (Accession NM\_012268) is another VGAM1959 host target gene. HU-K4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HU-K4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HU-K4 BINDING SITE, designated SEQ ID:14592, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67796] Another function of VGAM1959 is therefore inhibition of HU-K4 (Accession NM\_012268). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HU-K4. Integrin, Alpha 10 (ITGA10, Accession XM\_002097) is another VGAM1959 host target gene. ITGA10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by ITGA10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA10 BINDING SITE, designated SEQ ID:29861, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67797] Another function of VGAM1959 is therefore inhibition of Integrin, Alpha 10 (ITGA10, Accession XM\_002097). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA10. JM11 (Accession NM\_033626) is another VGAM1959 host target gene. JM11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JM11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JM11 BINDING SITE, designated SEQ ID:27331, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67798] Another function of VGAM1959 is therefore inhibition of JM11 (Accession NM\_033626). Accordingly, utilities of

VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JM11. Potassium Inwardly-rectifying Channel, Subfamily J, Member 9 (KCNJ9, Accession NM\_004983) is another VGAM1959 host target gene. KCNJ9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNJ9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ9 BINDING SITE, designated SEQ ID:11430, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67799] Another function of VGAM1959 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 9 (KCNJ9, Accession NM\_004983). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ9. Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM\_029962) is another VGAM1959 host target gene. KCNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNT1, corresponding to a HOST TARGET



binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNT1 BINDING SITE, designated SEQ ID:30978, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67800] Another function of VGAM1959 is therefore inhibition of Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM\_029962). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNT1. KH Domain Containing, RNA Binding, Signal Transduction Associated 1 (KHDRBS1, Accession NM\_006559) is another VGAM1959 host target gene. KHDRBS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KHDRBS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KHDRBS1 BINDING SITE, designated SEQ ID:13330, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67801] Another function of VGAM1959 is therefore inhibition of

KH Domain Containing, RNA Binding, Signal Transduction Associated 1 (KHDRBS1, Accession NM\_006559). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KHDRBS1. KIAA0052 (Accession XM\_042108) is another VGAM1959 host target gene. KIAA0052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0052 BINDING SITE, designated SEQ ID:33692, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67802] Another function of VGAM1959 is therefore inhibition of KIAA0052 (Accession XM\_042108). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0052. KIAA0057 (Accession NM\_012288) is another VGAM1959 host target gene. KIAA0057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0057, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0057 BINDING SITE, designated SEQ ID:14618, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67803] Another function of VGAM1959 is therefore inhibition of KIAA0057 (Accession NM\_012288). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0057. KIAA0087 (Accession NM\_014769) is another VGAM1959 host target gene. KIAA0087 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0087, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0087 BINDING SITE, designated SEQ ID:16557, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67804] Another function of VGAM1959 is therefore inhibition of KIAA0087 (Accession NM\_014769). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0087. KIAA0140 (Accession NM\_014661) is another VGAM1959 host target gene. KIAA0140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0140 BINDING SITE, designated SEQ ID:16108, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67805] Another function of VGAM1959 is therefore inhibition of KIAA0140 (Accession NM\_014661). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0140. KIAA0146 (Accession XM\_088282) is another VGAM1959 host target gene. KIAA0146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0146 BINDING SITE, designated SEQ ID:39584, to the nucleotide sequence of VGAM1959 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4670.

[67806] Another function of VGAM1959 is therefore inhibition of KIAA0146 (Accession XM\_088282). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0146. KIAA0218 (Accession NM\_014760) is another VGAM1959 host target gene. KIAA0218 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0218 BINDING SITE, designated SEQ ID:16519, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67807] Another function of VGAM1959 is therefore inhibition of KIAA0218 (Accession NM\_014760). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0218. KIAA0247 (Accession NM\_014734) is another VGAM1959 host target gene. KIAA0247 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0247, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0247 BINDING SITE, designated SEQ ID:16374, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67808] Another function of VGAM1959 is therefore inhibition of KIAA0247 (Accession NM\_014734). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0247. KIAA0261 (Accession XM\_042946) is another VGAM1959 host target gene. KIAA0261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0261 BINDING SITE, designated SEQ ID:33838, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67809] Another function of VGAM1959 is therefore inhibition of KIAA0261 (Accession XM\_042946). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0261. KIAA0286 (Accession XM\_043118) is another VGAM1959 host target gene. KIAA0286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0286 BINDING SITE, designated SEQ ID:33909, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67810] Another function of VGAM1959 is therefore inhibition of KIAA0286 (Accession XM\_043118). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0286. KIAA0316 (Accession XM\_045712) is another VGAM1959 host target gene. KIAA0316 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0316, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0316 BINDING SITE, designated SEQ ID:34531, to the

nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67811] Another function of VGAM1959 is therefore inhibition of KIAA0316 (Accession XM\_045712). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0316. KIAA0323 (Accession XM\_032634) is another VGAM1959 host target gene. KIAA0323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0323 BINDING SITE, designated SEQ ID:31691, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67812] Another function of VGAM1959 is therefore inhibition of KIAA0323 (Accession XM\_032634). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0323. KIAA0326 (Accession XM\_034819) is another VGAM1959 host target gene. KIAA0326 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by KIAA0326, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0326 BINDING SITE, designated SEQ ID:32160, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67813] Another function of VGAM1959 is therefore inhibition of KIAA0326 (Accession XM\_034819). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0326. KIAA0342 (Accession XM\_047357) is another VGAM1959 host target gene. KIAA0342 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0342 BINDING SITE, designated SEQ ID:34961, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67814] Another function of VGAM1959 is therefore inhibition of KIAA0342 (Accession XM\_047357). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0342. KIAA0418 (Accession NM\_014631) is another VGAM1959 host target gene. KIAA0418 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0418 BINDING SITE, designated SEQ ID:15999, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67815] Another function of VGAM1959 is therefore inhibition of KIAA0418 (Accession NM\_014631). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0418. KIAA0444 (Accession XM\_030999) is another VGAM1959 host target gene. KIAA0444 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0444, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0444 BINDING SITE, designated SEQ ID:31240, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67816] Another function of VGAM1959 is therefore inhibition of KIAA0444 (Accession XM\_030999). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0444. KIAA0450 (Accession NM\_014638) is another VGAM1959 host target gene. KIAA0450 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0450 BINDING SITE, designated SEQ ID:16033, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67817] Another function of VGAM1959 is therefore inhibition of KIAA0450 (Accession NM\_014638). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0450. KIAA0469 (Accession NM\_014851) is another VGAM1959 host target gene. KIAA0469 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0469, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0469 BINDING SITE, designated SEQ ID:16889, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67818] Another function of VGAM1959 is therefore inhibition of KIAA0469 (Accession NM\_014851). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0469. KIAA0495 (Accession XM\_031397) is another VGAM1959 host target gene. KIAA0495 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0495 BINDING SITE, designated SEQ ID:31357, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67819] Another function of VGAM1959 is therefore inhibition of

KIAA0495 (Accession XM\_031397). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0495. KIAA0514 (Accession NM\_014696) is another VGAM1959 host target gene. KIAA0514 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0514 BINDING SITE, designated SEQ ID:16205, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67820] Another function of VGAM1959 is therefore inhibition of KIAA0514 (Accession NM\_014696). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0514. KIAA0775 (Accession NM\_014726) is another VGAM1959 host target gene. KIAA0775 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0775, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0775 BINDING SITE, designated SEQ ID:16321, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67821] Another function of VGAM1959 is therefore inhibition of KIAA0775 (Accession NM\_014726). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0775. KIAA0794 (Accession XM\_087353) is another VGAM1959 host target gene. KIAA0794 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0794 BINDING SITE, designated SEQ ID:39186, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67822] Another function of VGAM1959 is therefore inhibition of KIAA0794 (Accession XM\_087353). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0794. KIAA0802 (Accession XM\_031357) is another

VGAM1959 host target gene. KIAA0802 BINDING SITE1 and KIAA0802 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0802, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0802 BINDING SITE1 and KIAA0802 BINDING SITE2, designated SEQ ID:31350 and SEQ ID:31353 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67823] Another function of VGAM1959 is therefore inhibition of KIAA0802 (Accession XM\_031357). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0802. KIAA0918 (Accession XM\_054869) is another VGAM1959 host target gene. KIAA0918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0918 BINDING SITE, designated SEQ ID:36198, to the

nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67824] Another function of VGAM1959 is therefore inhibition of KIAA0918 (Accession XM\_054869). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0918. KIAA0924 (Accession NM\_014897) is another VGAM1959 host target gene. KIAA0924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0924 BINDING SITE, designated SEQ ID:17064, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67825] Another function of VGAM1959 is therefore inhibition of KIAA0924 (Accession NM\_014897). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0924. KIAA0939 (Accession XM\_030524) is another VGAM1959 host target gene. KIAA0939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by KIAA0939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0939 BINDING SITE, designated SEQ ID:31064, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67826] Another function of VGAM1959 is therefore inhibition of KIAA0939 (Accession XM\_030524). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0939. KIAA0945 (Accession NM\_014952) is another VGAM1959 host target gene. KIAA0945 BINDING SITE1 and KIAA0945 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0945, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0945 BINDING SITE1 and KIAA0945 BINDING SITE2, designated SEQ ID:17292 and SEQ ID:17293 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67827] Another function of VGAM1959 is therefore inhibition of KIAA0945 (Accession NM\_014952). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0945. KIAA0981 (Accession XM\_028867) is another VGAM1959 host target gene. KIAA0981 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0981 BINDING SITE, designated SEQ ID:30798, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67828] Another function of VGAM1959 is therefore inhibition of KIAA0981 (Accession XM\_028867). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0981. KIAA0982 (Accession NM\_014023) is another VGAM1959 host target gene. KIAA0982 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0982, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0982 BINDING SITE, designated SEQ ID:15249, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67829] Another function of VGAM1959 is therefore inhibition of KIAA0982 (Accession NM\_014023). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0982. KIAA1016 (Accession XM\_166260) is another VGAM1959 host target gene. KIAA1016 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1016 BINDING SITE, designated SEQ ID:44086, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67830] Another function of VGAM1959 is therefore inhibition of KIAA1016 (Accession XM\_166260). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1016. KIAA1024 (Accession XM\_044580) is another VGAM1959 host target gene. KIAA1024 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1024 BINDING SITE, designated SEQ ID:34238, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67831] Another function of VGAM1959 is therefore inhibition of KIAA1024 (Accession XM\_044580). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1024. KIAA1026 (Accession XM\_048825) is another VGAM1959 host target gene. KIAA1026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1026 BINDING SITE, designated SEQ ID:35280, to the nucleotide sequence of VGAM1959 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4670.

[67832] Another function of VGAM1959 is therefore inhibition of KIAA1026 (Accession XM\_048825). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1026. KIAA1032 (Accession XM\_038604) is another VGAM1959 host target gene. KIAA1032 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1032 BINDING SITE, designated SEQ ID:32877, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67833] Another function of VGAM1959 is therefore inhibition of KIAA1032 (Accession XM\_038604). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1032. KIAA1052 (Accession NM\_014956) is another VGAM1959 host target gene. KIAA1052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1052, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1052 BINDING SITE, designated SEQ ID:17311, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67834] Another function of VGAM1959 is therefore inhibition of KIAA1052 (Accession NM\_014956). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1052. KIAA1068 (Accession NM\_015332) is another VGAM1959 host target gene. KIAA1068 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1068, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1068 BINDING SITE, designated SEQ ID:17643, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67835] Another function of VGAM1959 is therefore inhibition of KIAA1068 (Accession NM\_015332). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1068. KIAA1130 (Accession XM\_031104) is another VGAM1959 host target gene. KIAA1130 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1130 BINDING SITE, designated SEQ ID:31283, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67836] Another function of VGAM1959 is therefore inhibition of KIAA1130 (Accession XM\_031104). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1130. KIAA1185 (Accession XM\_031399) is another VGAM1959 host target gene. KIAA1185 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1185, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1185 BINDING SITE, designated SEQ ID:31372, to the

nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67837] Another function of VGAM1959 is therefore inhibition of KIAA1185 (Accession XM\_031399). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1185. KIAA1190 (Accession XM\_048695) is another VGAM1959 host target gene. KIAA1190 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1190 BINDING SITE, designated SEQ ID:35224, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67838] Another function of VGAM1959 is therefore inhibition of KIAA1190 (Accession XM\_048695). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1190. KIAA1199 (Accession XM\_051860) is another VGAM1959 host target gene. KIAA1199 BINDING SITE is HOST TARGET binding site found in the 3' untranslated



region of mRNA encoded by KIAA1199, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1199 BINDING SITE, designated SEQ ID:35900, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67839] Another function of VGAM1959 is therefore inhibition of KIAA1199 (Accession XM\_051860). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1199. KIAA1233 (Accession XM\_032181) is another VGAM1959 host target gene. KIAA1233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1233 BINDING SITE, designated SEQ ID:31589, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67840] Another function of VGAM1959 is therefore inhibition of KIAA1233 (Accession XM\_032181). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1233. KIAA1247 (Accession XM\_030036) is another VGAM1959 host target gene. KIAA1247 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1247 BINDING SITE, designated SEQ ID:30988, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67841] Another function of VGAM1959 is therefore inhibition of KIAA1247 (Accession XM\_030036). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1247. KIAA1280 (Accession XM\_045766) is another VGAM1959 host target gene. KIAA1280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1280 BINDING SITE, designated SEQ ID:34553, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67842] Another function of VGAM1959 is therefore inhibition of KIAA1280 (Accession XM\_045766). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1280. KIAA1322 (Accession XM\_052626) is another VGAM1959 host target gene. KIAA1322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1322 BINDING SITE, designated SEQ ID:36023, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67843] Another function of VGAM1959 is therefore inhibition of KIAA1322 (Accession XM\_052626). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1322. KIAA1332 (Accession XM\_048774) is another VGAM1959 host target gene. KIAA1332 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1332 BINDING SITE, designated SEQ ID:35255, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67844] Another function of VGAM1959 is therefore inhibition of KIAA1332 (Accession XM\_048774). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1332. KIAA1399 (Accession XM\_046685) is another VGAM1959 host target gene. KIAA1399 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1399 BINDING SITE, designated SEQ ID:34796, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67845] Another function of VGAM1959 is therefore inhibition of

KIAA1399 (Accession XM\_046685). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1399. KIAA1449 (Accession NM\_020839) is another VGAM1959 host target gene. KIAA1449 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1449 BINDING SITE, designated SEQ ID:21899, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67846] Another function of VGAM1959 is therefore inhibition of KIAA1449 (Accession NM\_020839). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1449. KIAA1458 (Accession XM\_044434) is another VGAM1959 host target gene. KIAA1458 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1458, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1458 BINDING SITE, designated SEQ ID:34204, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67847] Another function of VGAM1959 is therefore inhibition of KIAA1458 (Accession XM\_044434). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1458. KIAA1465 (Accession XM\_027396) is another VGAM1959 host target gene. KIAA1465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1465 BINDING SITE, designated SEQ ID:30502, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67848] Another function of VGAM1959 is therefore inhibition of KIAA1465 (Accession XM\_027396). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1465. KIAA1467 (Accession XM\_049605) is another

VGAM1959 host target gene. KIAA1467 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1467, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1467 BINDING SITE, designated SEQ ID:35451, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67849] Another function of VGAM1959 is therefore inhibition of KIAA1467 (Accession XM\_049605). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1467. KIAA1509 (Accession XM\_029353) is another VGAM1959 host target gene. KIAA1509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1509 BINDING SITE, designated SEQ ID:30877, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67850] Another function of VGAM1959 is therefore inhibition of KIAA1509 (Accession XM\_029353). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1509. KIAA1576 (Accession XM\_038186) is another VGAM1959 host target gene. KIAA1576 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1576 BINDING SITE, designated SEQ ID:32772, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67851] Another function of VGAM1959 is therefore inhibition of KIAA1576 (Accession XM\_038186). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1576. KIAA1580 (Accession XM\_045271) is another VGAM1959 host target gene. KIAA1580 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1580, corresponding to a HOST TARGET binding site such as BINDING SITE I,



BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1580 BINDING SITE, designated SEQ ID:34412, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67852] Another function of VGAM1959 is therefore inhibition of KIAA1580 (Accession XM\_045271). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1580. KIAA1656 (Accession XM\_038022) is another VGAM1959 host target gene. KIAA1656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1656 BINDING SITE, designated SEQ ID:32732, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67853] Another function of VGAM1959 is therefore inhibition of KIAA1656 (Accession XM\_038022). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1656. KIAA1679 (Accession XM\_046570) is another VGAM1959 host target gene. KIAA1679 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1679, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1679 BINDING SITE, designated SEQ ID:34754, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67854] Another function of VGAM1959 is therefore inhibition of KIAA1679 (Accession XM\_046570). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1679. KIAA1729 (Accession XM\_114418) is another VGAM1959 host target gene. KIAA1729 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1729, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1729 BINDING SITE, designated SEQ ID:42950, to the nucleotide sequence of VGAM1959 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4670.

[67855] Another function of VGAM1959 is therefore inhibition of KIAA1729 (Accession XM\_114418). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1729. KIAA1755 (Accession XM\_028810) is another VGAM1959 host target gene. KIAA1755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1755, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1755 BINDING SITE, designated SEQ ID:30752, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67856] Another function of VGAM1959 is therefore inhibition of KIAA1755 (Accession XM\_028810). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1755. KIAA1789 (Accession XM\_040486) is another VGAM1959 host target gene. KIAA1789 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1789, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1789 BINDING SITE, designated SEQ ID:33313, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67857] Another function of VGAM1959 is therefore inhibition of KIAA1789 (Accession XM\_040486). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1789. KIAA1798 (Accession XM\_027074) is another VGAM1959 host target gene. KIAA1798 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1798 BINDING SITE, designated SEQ ID:30401, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67858] Another function of VGAM1959 is therefore inhibition of KIAA1798 (Accession XM\_027074). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1798. KIAA1805 (Accession XM\_086976) is another VGAM1959 host target gene. KIAA1805 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1805, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1805 BINDING SITE, designated SEQ ID:39002, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67859] Another function of VGAM1959 is therefore inhibition of KIAA1805 (Accession XM\_086976). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1805. KIAA1870 (Accession NM\_032888) is another VGAM1959 host target gene. KIAA1870 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1870 BINDING SITE, designated SEQ ID:26709, to the

nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67860] Another function of VGAM1959 is therefore inhibition of KIAA1870 (Accession NM\_032888). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1870. KIAA1904 (Accession XM\_056282) is another VGAM1959 host target gene. KIAA1904 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1904, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1904 BINDING SITE, designated SEQ ID:36374, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67861] Another function of VGAM1959 is therefore inhibition of KIAA1904 (Accession XM\_056282). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1904. KIAA1906 (Accession XM\_055095) is another VGAM1959 host target gene. KIAA1906 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1906 BINDING SITE, designated SEQ ID:36229, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67862] Another function of VGAM1959 is therefore inhibition of KIAA1906 (Accession XM\_055095). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1906. KIAA1908 (Accession XM\_055834) is another VGAM1959 host target gene. KIAA1908 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1908 BINDING SITE, designated SEQ ID:36340, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67863] Another function of VGAM1959 is therefore inhibition of KIAA1908 (Accession XM\_055834). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1908. KIAA1924 (Accession XM\_057091) is another VGAM1959 host target gene. KIAA1924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1924 BINDING SITE, designated SEQ ID:36476, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67864] Another function of VGAM1959 is therefore inhibition of KIAA1924 (Accession XM\_057091). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1924. KIAA1941 (Accession XM\_059318) is another VGAM1959 host target gene. KIAA1941 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1941, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of



KIAA1941 BINDING SITE, designated SEQ ID:36954, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67865] Another function of VGAM1959 is therefore inhibition of KIAA1941 (Accession XM\_059318). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1941. KIAA1948 (Accession XM\_091984) is another VGAM1959 host target gene. KIAA1948 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1948, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1948 BINDING SITE, designated SEQ ID:40079, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67866] Another function of VGAM1959 is therefore inhibition of KIAA1948 (Accession XM\_091984). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1948. KIAA1950 (Accession XM\_166532) is another VGAM1959 host target gene. KIAA1950 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1950 BINDING SITE, designated SEQ ID:44486, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67867] Another function of VGAM1959 is therefore inhibition of KIAA1950 (Accession XM\_166532). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1950. KIAA1977 (Accession XM\_058800) is another VGAM1959 host target gene. KIAA1977 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1977 BINDING SITE, designated SEQ ID:36745, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67868] Another function of VGAM1959 is therefore inhibition of

KIAA1977 (Accession XM\_058800). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1977. KIAA1981 (Accession XM\_114000) is another VGAM1959 host target gene. KIAA1981 BINDING SITE1 and KIAA1981 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1981, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1981 BINDING SITE1 and KIAA1981 BINDING SITE2, designated SEQ ID:42608 and SEQ ID:42611 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67869] Another function of VGAM1959 is therefore inhibition of KIAA1981 (Accession XM\_114000). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1981. Kinesin Family Member 13B (KIF13B, Accession NM\_015254) is another VGAM1959 host target gene. KIF13B BINDING SITE1 and KIF13B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions

of mRNA encoded by KIF13B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF13B BINDING SITE1 and KIF13B BINDING SITE2, designated SEQ ID:17583 and SEQ ID:42788 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67870] Another function of VGAM1959 is therefore inhibition of Kinesin Family Member 13B (KIF13B, Accession NM\_015254). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF13B. LIM and SH3 Protein 1 (LASP1, Accession NM\_006148) is another VGAM1959 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LASP1 BINDING SITE, designated SEQ ID:12795, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67871] Another function of VGAM1959 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM\_006148). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. LATS, Large Tumor Suppressor, Homolog 1 (Drosophila) (LATS1, Accession XM\_015547) is another VGAM1959 host target gene. LATS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LATS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LATS1 BINDING SITE, designated SEQ ID:30239, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67872] Another function of VGAM1959 is therefore inhibition of LATS, Large Tumor Suppressor, Homolog 1 (Drosophila) (LATS1, Accession XM\_015547). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LATS1. LIM Domain Kinase 2 (LIMK2, Accession NM\_016733) is another VGAM1959 host target gene. LIMK2 BINDING

SITE1 and LIMK2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LIMK2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMK2 BINDING SITE1 and LIMK2 BINDING SITE2, designated SEQ ID:18784 and SEQ ID:12094 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67873] Another function of VGAM1959 is therefore inhibition of LIM Domain Kinase 2 (LIMK2, Accession NM\_016733). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMK2. Mitogen-activated Protein Kinase 8 Interacting Protein 2 (MAPK8IP2, Accession NM\_016431) is another VGAM1959 host target gene. MAPK8IP2 BINDING SITE1 through MAPK8IP2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPK8IP2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK8IP2 BINDING SITE1

through MAPK8IP2 BINDING SITE3, designated SEQ ID:18552, SEQ ID:14704 and SEQ ID:29155 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67874] Another function of VGAM1959 is therefore inhibition of Mitogen-activated Protein Kinase 8 Interacting Protein 2 (MAPK8IP2, Accession NM\_016431). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK8IP2. MGC10471 (Accession NM\_030818) is another VGAM1959 host target gene. MGC10471 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC10471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10471 BINDING SITE, designated SEQ ID:25147, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67875] Another function of VGAM1959 is therefore inhibition of MGC10471 (Accession NM\_030818). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC10471. MGC10715 (Accession NM\_024325) is another VGAM1959 host target gene. MGC10715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10715 BINDING SITE, designated SEQ ID:23614, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67876] Another function of VGAM1959 is therefore inhibition of MGC10715 (Accession NM\_024325). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10715. MGC12760 (Accession NM\_032723) is another VGAM1959 host target gene. MGC12760 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12760, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12760 BINDING SITE, designated SEQ ID:26448, to the nucleotide sequence of VGAM1959 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4670.

[67877] Another function of VGAM1959 is therefore inhibition of MGC12760 (Accession NM\_032723). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12760. MGC13114 (Accession NM\_032366) is another VGAM1959 host target gene. MGC13114 BINDING SITE1 and MGC13114 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MGC13114, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13114 BINDING SITE1 and MGC13114 BINDING SITE2, designated SEQ ID:26151 and SEQ ID:26152 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67878] Another function of VGAM1959 is therefore inhibition of MGC13114 (Accession NM\_032366). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13114. MGC15873 (Accession NM\_032920) is another VGAM1959 host target gene. MGC15873 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC15873, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15873 BINDING SITE, designated SEQ ID:26741, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67879] Another function of VGAM1959 is therefore inhibition of MGC15873 (Accession NM\_032920). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15873. MGC2306 (Accession NM\_032638) is another VGAM1959 host target gene. MGC2306 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC2306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2306 BINDING SITE, designated SEQ ID:26352, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67880] Another function of VGAM1959 is therefore inhibition of

MGC2306 (Accession NM\_032638). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2306. MGC2721 (Accession NM\_032737) is another VGAM1959 host target gene. MGC2721 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2721 BINDING SITE, designated SEQ ID:26462, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67881] Another function of VGAM1959 is therefore inhibition of MGC2721 (Accession NM\_032737). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2721. MGC3222 (Accession NM\_024334) is another VGAM1959 host target gene. MGC3222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC3222 BINDING SITE, designated SEQ ID:23643, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67882] Another function of VGAM1959 is therefore inhibition of MGC3222 (Accession NM\_024334). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3222. MGC4415 (Accession NM\_031484) is another VGAM1959 host target gene. MGC4415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4415 BINDING SITE, designated SEQ ID:25574, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67883] Another function of VGAM1959 is therefore inhibition of MGC4415 (Accession NM\_031484). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4415. MGC4796 (Accession XM\_029031) is another

VGAM1959 host target gene. MGC4796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4796 BINDING SITE, designated SEQ ID:30832, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67884] Another function of VGAM1959 is therefore inhibition of MGC4796 (Accession XM\_029031). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4796. MGC8407 (Accession NM\_024046) is another VGAM1959 host target gene. MGC8407 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC8407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC8407 BINDING SITE, designated SEQ ID:23480, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67885] Another function of VGAM1959 is therefore inhibition of MGC8407 (Accession NM\_024046). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC8407. MIDORI (Accession XM\_057651) is another VGAM1959 host target gene. MIDORI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIDORI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIDORI BINDING SITE, designated SEQ ID:36531, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67886] Another function of VGAM1959 is therefore inhibition of MIDORI (Accession XM\_057651). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIDORI. MRF2 (Accession XM\_084482) is another VGAM1959 host target gene. MRF2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MRF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRF2 BINDING SITE, designated SEQ ID:37601, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67887] Another function of VGAM1959 is therefore inhibition of MRF2 (Accession XM\_084482). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRF2. MY038 (Accession NM\_032626) is another VGAM1959 host target gene. MY038 BINDING SITE1 and MY038 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MY038, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MY038 BINDING SITE1 and MY038 BINDING SITE2, designated SEQ ID:26345 and SEQ ID:26346 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67888] Another function of VGAM1959 is therefore inhibition of MY038 (Accession NM\_032626). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MY038. NDRG Family Member 4 (NDRG4, Accession NM\_022910) is another VGAM1959 host target gene. NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NDRG4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2, designated SEQ ID:23212 and SEQ ID:21697 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67889] Another function of VGAM1959 is therefore inhibition of NDRG Family Member 4 (NDRG4, Accession NM\_022910). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG4. NUDEL (Accession NM\_030808) is another VGAM1959 host target gene. NUDEL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDEL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.



Table 2 illustrates the complementarity of the nucleotide sequences of NUDEL BINDING SITE, designated SEQ ID:25123, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67890] Another function of VGAM1959 is therefore inhibition of NUDEL (Accession NM\_030808). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUDEL. Nucleoredoxin (NXN, Accession NM\_022463) is another VGAM1959 host target gene. NXN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXN BINDING SITE, designated SEQ ID:22813, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67891] Another function of VGAM1959 is therefore inhibition of Nucleoredoxin (NXN, Accession NM\_022463). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with NXN. Ornithine Decarboxylase Antizyme 2 (OAZ2, Accession NM\_002537) is another VGAM1959 host target gene. OAZ2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAZ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAZ2 BINDING SITE, designated SEQ ID:8377, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67892] Another function of VGAM1959 is therefore inhibition of Ornithine Decarboxylase Antizyme 2 (OAZ2, Accession NM\_002537). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAZ2. Obscurin, Cytoskeletal Calmodulin and Titin-interacting RhoGEF (OBSCN, Accession XM\_047536) is another VGAM1959 host target gene. OBSCN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OBSCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OBSCN BINDING SITE, designated SEQ

ID:34989, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67893] Another function of VGAM1959 is therefore inhibition of Obscurin, Cytoskeletal Calmodulin and Titin-interacting RhoGEF (OBSCN, Accession XM\_047536). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OBSCN. Olfactomedin 3 (OLFM3, Accession XM\_088951) is another VGAM1959 host target gene. OLFM3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OLFM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OLFM3 BINDING SITE, designated SEQ ID:39962, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67894] Another function of VGAM1959 is therefore inhibition of Olfactomedin 3 (OLFM3, Accession XM\_088951). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with OLFM3. p25 (Accession NM\_007030) is another VGAM1959 host target gene. p25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by p25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of p25 BINDING SITE, designated SEQ ID:13891, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67895] Another function of VGAM1959 is therefore inhibition of p25 (Accession NM\_007030). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with p25. Purinergic Receptor P2X-like 1, Orphan Receptor (P2RXL1, Accession NM\_005446) is another VGAM1959 host target gene. P2RXL1 BINDING SITE1 and P2RXL1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by P2RXL1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RXL1 BINDING SITE1 and P2RXL1 BINDING SITE2, designated SEQ

ID:11930 and SEQ ID:11934 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67896] Another function of VGAM1959 is therefore inhibition of Purinergic Receptor P2X-like 1, Orphan Receptor (P2RXL1, Accession NM\_005446). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RXL1. PC2 (positive cofactor 2, multiprotein complex) Glutamine/Q-rich-associated Protein (PCQAP, Accession NM\_015889) is another VGAM1959 host target gene. PC-QAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCQAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCQAP BINDING SITE, designated SEQ ID:18035, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67897] Another function of VGAM1959 is therefore inhibition of PC2 (positive cofactor 2, multiprotein complex) Glutamine/Q-rich-associated Protein (PCQAP, Accession

NM\_015889). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCQAP. Phosphodiesterase 11A (PDE11A, Accession NM\_016953) is another VGAM1959 host target gene. PDE11A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE11A BINDING SITE, designated SEQ ID:18867, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67898] Another function of VGAM1959 is therefore inhibition of Phosphodiesterase 11A (PDE11A, Accession NM\_016953). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE11A. Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession NM\_014644) is another VGAM1959 host target gene. PDE4DIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4DIP, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4DIP BINDING SITE, designated SEQ ID:16051, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67899] Another function of VGAM1959 is therefore inhibition of Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession NM\_014644). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4DIP. PIF1 (Accession XM\_027898) is another VGAM1959 host target gene. PIF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIF1 BINDING SITE, designated SEQ ID:30587, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67900] Another function of VGAM1959 is therefore inhibition of PIF1 (Accession XM\_027898). Accordingly, utilities of

VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIF1. PTEN Induced Putative Kinase 1 (PINK1, Accession NM\_032409) is another VGAM1959 host target gene. PINK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PINK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PINK1 BINDING SITE, designated SEQ ID:26194, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67901] Another function of VGAM1959 is therefore inhibition of PTEN Induced Putative Kinase 1 (PINK1, Accession NM\_032409). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PINK1. Phosphatidylserine Decarboxylase (PISD, Accession NM\_014338) is another VGAM1959 host target gene. PISD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PISD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity



of the nucleotide sequences of PISD BINDING SITE, designated SEQ ID:15655, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67902] Another function of VGAM1959 is therefore inhibition of Phosphatidylserine Decarboxylase (PISD, Accession NM\_014338). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PISD. Phospholipase C-like 2 (PLCL2, Accession XM\_042836) is another VGAM1959 host target gene. PLCL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLCL2 BINDING SITE, designated SEQ ID:33796, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67903] Another function of VGAM1959 is therefore inhibition of Phospholipase C-like 2 (PLCL2, Accession XM\_042836). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with PLCL2. PM5 (Accession XM\_027359) is another VGAM1959 host target gene. PM5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PM5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PM5 BINDING SITE, designated SEQ ID:30498, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67904] Another function of VGAM1959 is therefore inhibition of PM5 (Accession XM\_027359). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PM5. PP3501 (Accession NM\_021731) is another VGAM1959 host target gene. PP3501 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PP3501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP3501 BINDING SITE, designated SEQ ID:22333, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4670.

[67905] Another function of VGAM1959 is therefore inhibition of PP3501 (Accession NM\_021731). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP3501. PTPRF Interacting Protein, Binding Protein 1 (liprin beta 1) (PPFIBP1, Accession NM\_003622) is another VGAM1959 host target gene. PPFIBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPFIBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPFIBP1 BINDING SITE, designated SEQ ID:9686, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67906] Another function of VGAM1959 is therefore inhibition of PTPRF Interacting Protein, Binding Protein 1 (liprin beta 1) (PPFIBP1, Accession NM\_003622). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPFIBP1. Protein Phosphatase 4, Regulatory Subunit 1-like (PPP4R1L, Accession XM\_086650) is another VGAM1959

host target gene. PPP4R1L BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PPP4R1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP4R1L BINDING SITE, designated SEQ ID:38817, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67907] Another function of VGAM1959 is therefore inhibition of Protein Phosphatase 4, Regulatory Subunit 1-like (PPP4R1L, Accession XM\_086650). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP4R1L. Protein Regulator of Cytokinesis 1 (PRC1, Accession NM\_003981) is another VGAM1959 host target gene. PRC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRC1 BINDING SITE, designated SEQ ID:10120, to the nucleotide sequence of VGAM1959 RNA, herein

designated VGAM RNA, also designated SEQ ID:4670.

[67908] Another function of VGAM1959 is therefore inhibition of Protein Regulator of Cytokinesis 1 (PRC1, Accession NM\_003981). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRC1. PRO2405 (Accession NM\_018627) is another VGAM1959 host target gene. PRO2405 BINDING SITE1 and PRO2405 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PRO2405, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2405 BINDING SITE1 and PRO2405 BINDING SITE2, designated SEQ ID:20698 and SEQ ID:20699 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67909] Another function of VGAM1959 is therefore inhibition of PRO2405 (Accession NM\_018627). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2405. PRRDH (Accession NM\_015725) is another VGAM1959 host target gene. PRRDH BINDING SITE1 and

PRRDH BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PRRDH, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRRDH BINDING SITE1 and PRRDH BINDING SITE2, designated SEQ ID:17935 and SEQ ID:17936 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67910] Another function of VGAM1959 is therefore inhibition of PRRDH (Accession NM\_015725). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRRDH. Protein Tyrosine Phosphatase, Receptor Type, R (PTPRR, Accession NM\_002849) is another VGAM1959 host target gene. PTPRR BINDING SITE1 and PTPRR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRR BINDING SITE1 and PTPRR BINDING SITE2, designated SEQ ID:8743 and

SEQ ID:8697 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67911] Another function of VGAM1959 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, R (PTPRR, Accession NM\_002849). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRR. RAB3D, Member RAS Oncogene Family (RAB3D, Accession NM\_004283) is another VGAM1959 host target gene. RAB3D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB3D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB3D BINDING SITE, designated SEQ ID:10495, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67912] Another function of VGAM1959 is therefore inhibition of RAB3D, Member RAS Oncogene Family (RAB3D, Accession NM\_004283). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with RAB3D. RAI (Accession NM\_006663) is another VGAM1959 host target gene. RAI BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI BINDING SITE, designated SEQ ID:13469, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67913] Another function of VGAM1959 is therefore inhibition of RAI (Accession NM\_006663). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI. Retinoic Acid Induced 17 (RAI17, Accession XM\_166091) is another VGAM1959 host target gene. RAI17 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAI17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI17 BINDING SITE, designated SEQ ID:43864, to the nucleotide sequence of VGAM1959 RNA, herein designated



VGAM RNA, also designated SEQ ID:4670.

[67914] Another function of VGAM1959 is therefore inhibition of Retinoic Acid Induced 17 (RAI17, Accession XM\_166091). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI17. RAS Guanyl Releasing Protein 4 (RASGRP4, Accession NM\_052949) is another VGAM1959 host target gene. RASGRP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASGRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASGRP4 BINDING SITE, designated SEQ ID:27506, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67915] Another function of VGAM1959 is therefore inhibition of RAS Guanyl Releasing Protein 4 (RASGRP4, Accession NM\_052949). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASGRP4. Regulator of G-protein Signalling 12 (RGS12, Accession NM\_002926) is another VGAM1959 host target gene. RGS12 BINDING SITE

is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RGS12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS12 BINDING SITE, designated SEQ ID:8830, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67916] Another function of VGAM1959 is therefore inhibition of Regulator of G-protein Signalling 12 (RGS12, Accession NM\_002926). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS12. RLUC (Accession NM\_058192) is another VGAM1959 host target gene. RLUC BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RLUC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RLUC BINDING SITE, designated SEQ ID:27754, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67917] Another function of VGAM1959 is therefore inhibition of RLUC (Accession NM\_058192). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RLUC. RPP14 (Accession XM\_003044) is another VGAM1959 host target gene. RPP14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPP14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPP14 BINDING SITE, designated SEQ ID:29926, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67918] Another function of VGAM1959 is therefore inhibition of RPP14 (Accession XM\_003044). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPP14. SAM Domain and HD Domain 1 (SAMHD1, Accession XM\_028704) is another VGAM1959 host target gene. SAMHD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SAMHD1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SAMHD1 BINDING SITE, designated SEQ ID:30737, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67919] Another function of VGAM1959 is therefore inhibition of SAM Domain and HD Domain 1 (SAMHD1, Accession XM\_028704). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAMHD1. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM\_004263) is another VGAM1959 host target gene. SEMA4F BINDING SITE1 and SEMA4F BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SEMA4F, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4F BINDING SITE1 and SEMA4F BINDING SITE2, designated SEQ ID:10456 and SEQ ID:10458 respectively, to the nucleotide sequence of VGAM1959 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4670.

[67920] Another function of VGAM1959 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM\_004263). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4F. Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM\_144564) is another VGAM1959 host target gene. SLC39A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC39A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC39A3 BINDING SITE, designated SEQ ID:29357, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67921] Another function of VGAM1959 is therefore inhibition of Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM\_144564). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

SLC39A3. SMC1 Structural Maintenance of Chromosomes 1-like 1 (yeast) (SMC1L1, Accession XM\_050403) is another VGAM1959 host target gene. SMC1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMC1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMC1L1 BINDING SITE, designated SEQ ID:35618, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67922] Another function of VGAM1959 is therefore inhibition of SMC1 Structural Maintenance of Chromosomes 1-like 1 (yeast) (SMC1L1, Accession XM\_050403). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMC1L1. Syntrophin, Gamma 1 (SNTG1, Accession NM\_018967) is another VGAM1959 host target gene. SNTG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNTG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of SNTG1 BINDING SITE, designated SEQ ID:21041, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67923] Another function of VGAM1959 is therefore inhibition of Syntrophin, Gamma 1 (SNTG1, Accession NM\_018967). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNTG1. SR-BP1 (Accession NM\_005866) is another VGAM1959 host target gene. SR-BP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SR-BP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SR-BP1 BINDING SITE, designated SEQ ID:12485, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67924] Another function of VGAM1959 is therefore inhibition of SR-BP1 (Accession NM\_005866). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SR-BP1.

SSB-3 (Accession NM\_080861) is another VGAM1959 host target gene. SSB-3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SSB-3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSB-3 BINDING SITE, designated SEQ ID:28102, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67925] Another function of VGAM1959 is therefore inhibition of SSB-3 (Accession NM\_080861). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSB-3. SSH2 (Accession XM\_030846) is another VGAM1959 host target gene. SSH2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSH2 BINDING SITE, designated SEQ ID:31190, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ



ID:4670.

[67926] Another function of VGAM1959 is therefore inhibition of SSH2 (Accession XM\_030846). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH2. Syntaxin 3A (STX3A, Accession NM\_004177) is another VGAM1959 host target gene. STX3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STX3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STX3A BINDING SITE, designated SEQ ID:10387, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67927] Another function of VGAM1959 is therefore inhibition of Syntaxin 3A (STX3A, Accession NM\_004177). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STX3A. Sulfotransferase Family, Cytosolic, 1C, Member 2 (SULT1C2, Accession NM\_006588) is another VGAM1959 host target gene. SULT1C2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by SULT1C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SULT1C2 BINDING SITE, designated SEQ ID:13353, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67928] Another function of VGAM1959 is therefore inhibition of Sulfotransferase Family, Cytosolic, 1C, Member 2 (SULT1C2, Accession NM\_006588). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SULT1C2. T-box 4 (TBX4, Accession NM\_018488) is another VGAM1959 host target gene. TBX4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBX4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBX4 BINDING SITE, designated SEQ ID:20546, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67929] Another function of VGAM1959 is therefore inhibition of

T-box 4 (TBX4, Accession NM\_018488). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBX4. Testis Expressed Sequence 27 (TEX27, Accession NM\_021943) is another VGAM1959 host target gene. TEX27 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEX27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEX27 BINDING SITE, designated SEQ ID:22459, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67930] Another function of VGAM1959 is therefore inhibition of Testis Expressed Sequence 27 (TEX27, Accession NM\_021943). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEX27. Tigger Transposable Element Derived 1 (TIGD1, Accession XM\_114293) is another VGAM1959 host target gene. TIGD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TIGD1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIGD1 BINDING SITE, designated SEQ ID:42848, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67931] Another function of VGAM1959 is therefore inhibition of Tigger Transposable Element Derived 1 (TIGD1, Accession XM\_114293). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIGD1. Tumor Necrosis Factor, Alpha-induced Protein 3 (TNFAIP3, Accession NM\_006290) is another VGAM1959 host target gene. TNFAIP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFAIP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFAIP3 BINDING SITE, designated SEQ ID:12979, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67932] Another function of VGAM1959 is therefore inhibition of

Tumor Necrosis Factor, Alpha-induced Protein 3 (TNFAIP3, Accession NM\_006290). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFAIP3. Three Prime Repair Exonuclease 1 (TREX1, Accession NM\_016381) is another VGAM1959 host target gene. TREX1 BINDING SITE1 through TREX1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TREX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TREX1 BINDING SITE1 through TREX1 BINDING SITE3, designated SEQ ID:18521, SEQ ID:27341 and SEQ ID:27348 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67933] Another function of VGAM1959 is therefore inhibition of Three Prime Repair Exonuclease 1 (TREX1, Accession NM\_016381). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TREX1. UBCE7IP5 (Accession NM\_014948) is another VGAM1959 host target gene. UBCE7IP5 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by UBCE7IP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBCE7IP5 BINDING SITE, designated SEQ ID:17271, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67934] Another function of VGAM1959 is therefore inhibition of UBCE7IP5 (Accession NM\_014948). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBCE7IP5. UDP-glucuronate Decarboxylase 1 (UXS1, Accession NM\_025076) is another VGAM1959 host target gene. UXS1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by UXS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UXS1 BINDING SITE, designated SEQ ID:24677, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67935] Another function of VGAM1959 is therefore inhibition of

UDP-glucuronate Decarboxylase 1 (UXS1, Accession NM\_025076). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UXS1. VI (Accession NM\_013443) is another VGAM1959 host target gene. VI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VI BINDING SITE, designated SEQ ID:15110, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67936] Another function of VGAM1959 is therefore inhibition of VI (Accession NM\_013443). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VI. VLCS-H1 (Accession NM\_014031) is another VGAM1959 host target gene. VLCS-H1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by VLCS-H1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of VLCS-H1 BINDING SITE, designated SEQ ID:15260, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67937] Another function of VGAM1959 is therefore inhibition of VLCS-H1 (Accession NM\_014031). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VLCS-H1. WD Repeat Domain 7 (WDR7, Accession NM\_015285) is another VGAM1959 host target gene. WDR7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WDR7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WDR7 BINDING SITE, designated SEQ ID:17610, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67938] Another function of VGAM1959 is therefore inhibition of WD Repeat Domain 7 (WDR7, Accession NM\_015285). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WDR7. Zinc Finger, DHHC Domain Con-



taining 8 (ZDHHC8, Accession XM\_033828) is another VGAM1959 host target gene. ZDHHC8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZDHHC8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC8 BINDING SITE, designated SEQ ID:31962, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67939] Another function of VGAM1959 is therefore inhibition of Zinc Finger, DHHC Domain Containing 8 (ZDHHC8, Accession XM\_033828). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC8. Zinc Finger Protein 95 Homolog (mouse) (ZFP95, Accession NM\_014569) is another VGAM1959 host target gene. ZFP95 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZFP95, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP95 BINDING SITE, designated SEQ

ID:15923, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67940] Another function of VGAM1959 is therefore inhibition of Zinc Finger Protein 95 Homolog (mouse) (ZFP95, Accession NM\_014569). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP95. ZID (Accession NM\_006626) is another VGAM1959 host target gene. ZID BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZID, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZID BINDING SITE, designated SEQ ID:13416, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67941] Another function of VGAM1959 is therefore inhibition of ZID (Accession NM\_006626). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZID. Zinc Finger Protein 17 (HPF3, KOX 10) (ZNF17, Accession XM\_091895) is another VGAM1959 host target gene.

ZNF17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF17 BINDING SITE, designated SEQ ID:40070, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67942] Another function of VGAM1959 is therefore inhibition of Zinc Finger Protein 17 (HPF3, KOX 10) (ZNF17, Accession XM\_091895). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF17. Zinc Finger Protein 317 (ZNF317, Accession XM\_050435) is another VGAM1959 host target gene. ZNF317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF317 BINDING SITE, designated SEQ ID:35635, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM

RNA, also designated SEQ ID:4670.

[67943] Another function of VGAM1959 is therefore inhibition of Zinc Finger Protein 317 (ZNF317, Accession XM\_050435). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF317. LOC115051 (Accession XM\_010647) is another VGAM1959 host target gene. LOC115051 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115051 BINDING SITE, designated SEQ ID:30161, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67944] Another function of VGAM1959 is therefore inhibition of LOC115051 (Accession XM\_010647). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115051. LOC115110 (Accession XM\_049825) is another VGAM1959 host target gene. LOC115110 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC115110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115110 BINDING SITE, designated SEQ ID:35509, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67945] Another function of VGAM1959 is therefore inhibition of LOC115110 (Accession XM\_049825). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115110. LOC115343 (Accession XM\_050640) is another VGAM1959 host target gene. LOC115343 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115343, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115343 BINDING SITE, designated SEQ ID:35666, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67946] Another function of VGAM1959 is therefore inhibition of LOC115343 (Accession XM\_050640). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115343. LOC115708 (Accession XM\_056552) is another VGAM1959 host target gene. LOC115708 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115708, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115708 BINDING SITE, designated SEQ ID:36405, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67947] Another function of VGAM1959 is therefore inhibition of LOC115708 (Accession XM\_056552). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115708. LOC120772 (Accession XM\_058505) is another VGAM1959 host target gene. LOC120772 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC120772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC120772 BINDING SITE, designated SEQ ID:36628, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67948] Another function of VGAM1959 is therefore inhibition of LOC120772 (Accession XM\_058505). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120772. LOC122792 (Accession NM\_145251) is another VGAM1959 host target gene. LOC122792 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122792, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122792 BINDING SITE, designated SEQ ID:29763, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67949] Another function of VGAM1959 is therefore inhibition of LOC122792 (Accession NM\_145251). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122792. LOC124145 (Accession XM\_058775) is another VGAM1959 host target gene. LOC124145 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC124145, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124145 BINDING SITE, designated SEQ ID:36735, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67950] Another function of VGAM1959 is therefore inhibition of LOC124145 (Accession XM\_058775). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124145. LOC124245 (Accession NM\_144604) is another VGAM1959 host target gene. LOC124245 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC124245, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124245 BINDING SITE, designated SEQ ID:29418, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67951] Another function of VGAM1959 is therefore inhibition of



LOC124245 (Accession NM\_144604). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124245. LOC124538 (Accession XM\_064177) is another VGAM1959 host target gene. LOC124538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124538 BINDING SITE, designated SEQ ID:37257, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67952] Another function of VGAM1959 is therefore inhibition of LOC124538 (Accession XM\_064177). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124538. LOC124842 (Accession XM\_064333) is another VGAM1959 host target gene. LOC124842 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC124842 BINDING SITE, designated SEQ ID:37259, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67953] Another function of VGAM1959 is therefore inhibition of LOC124842 (Accession XM\_064333). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124842. LOC126917 (Accession XM\_059091) is another VGAM1959 host target gene. LOC126917 BINDING SITE1 and LOC126917 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC126917, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126917 BINDING SITE1 and LOC126917 BINDING SITE2, designated SEQ ID:36874 and SEQ ID:36875 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67954] Another function of VGAM1959 is therefore inhibition of LOC126917 (Accession XM\_059091). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC126917. LOC132671 (Accession NM\_145263) is another VGAM1959 host target gene. LOC132671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC132671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132671 BINDING SITE, designated SEQ ID:29776, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67955] Another function of VGAM1959 is therefore inhibition of LOC132671 (Accession NM\_145263). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132671. LOC133308 (Accession XM\_059638) is another VGAM1959 host target gene. LOC133308 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC133308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133308 BINDING SITE, designated SEQ ID:37036, to

the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67956] Another function of VGAM1959 is therefore inhibition of LOC133308 (Accession XM\_059638). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133308. LOC133923 (Accession XM\_068602) is another VGAM1959 host target gene. LOC133923 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC133923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133923 BINDING SITE, designated SEQ ID:37382, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67957] Another function of VGAM1959 is therefore inhibition of LOC133923 (Accession XM\_068602). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133923. LOC139296 (Accession XM\_066612) is another VGAM1959 host target gene. LOC139296 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC139296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139296 BINDING SITE, designated SEQ ID:37339, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67958] Another function of VGAM1959 is therefore inhibition of LOC139296 (Accession XM\_066612). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139296. LOC143146 (Accession XM\_011844) is another VGAM1959 host target gene. LOC143146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143146 BINDING SITE, designated SEQ ID:30195, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67959] Another function of VGAM1959 is therefore inhibition of LOC143146 (Accession XM\_011844). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143146. LOC143279 (Accession XM\_084476) is another VGAM1959 host target gene. LOC143279 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143279, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143279 BINDING SITE, designated SEQ ID:37600, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67960] Another function of VGAM1959 is therefore inhibition of LOC143279 (Accession XM\_084476). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143279. LOC143425 (Accession XM\_113695) is another VGAM1959 host target gene. LOC143425 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC143425 BINDING SITE, designated SEQ ID:42352, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67961] Another function of VGAM1959 is therefore inhibition of LOC143425 (Accession XM\_113695). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143425. LOC143719 (Accession XM\_027090) is another VGAM1959 host target gene. LOC143719 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143719 BINDING SITE, designated SEQ ID:30405, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67962] Another function of VGAM1959 is therefore inhibition of LOC143719 (Accession XM\_027090). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143719. LOC144182 (Accession NM\_139136) is another VGAM1959 host target gene. LOC144182 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144182 BINDING SITE, designated SEQ ID:29167, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67963] Another function of VGAM1959 is therefore inhibition of LOC144182 (Accession NM\_139136). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144182. LOC144266 (Accession XM\_084795) is another VGAM1959 host target gene. LOC144266 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144266 BINDING SITE, designated SEQ ID:37709, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67964] Another function of VGAM1959 is therefore inhibition of



LOC144266 (Accession XM\_084795). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144266. LOC144305 (Accession XM\_096572) is another VGAM1959 host target gene. LOC144305 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144305 BINDING SITE, designated SEQ ID:40399, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67965] Another function of VGAM1959 is therefore inhibition of LOC144305 (Accession XM\_096572). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144305. LOC144317 (Accession XM\_084813) is another VGAM1959 host target gene. LOC144317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC144317 BINDING SITE, designated SEQ ID:37717, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67966] Another function of VGAM1959 is therefore inhibition of LOC144317 (Accession XM\_084813). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144317. LOC144501 (Accession XM\_096612) is another VGAM1959 host target gene. LOC144501 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144501 BINDING SITE, designated SEQ ID:40427, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67967] Another function of VGAM1959 is therefore inhibition of LOC144501 (Accession XM\_096612). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144501. LOC144535 (Accession XM\_084892) is an-

other VGAM1959 host target gene. LOC144535 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144535 BINDING SITE, designated SEQ ID:37762, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67968] Another function of VGAM1959 is therefore inhibition of LOC144535 (Accession XM\_084892). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144535. LOC144871 (Accession XM\_096698) is another VGAM1959 host target gene. LOC144871 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144871 BINDING SITE, designated SEQ ID:40468, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67969] Another function of VGAM1959 is therefore inhibition of LOC144871 (Accession XM\_096698). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144871. LOC145317 (Accession XM\_096760) is another VGAM1959 host target gene. LOC145317 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145317 BINDING SITE, designated SEQ ID:40530, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67970] Another function of VGAM1959 is therefore inhibition of LOC145317 (Accession XM\_096760). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145317. LOC145622 (Accession XM\_085186) is another VGAM1959 host target gene. LOC145622 BINDING SITE1 through LOC145622 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC145622, corresponding to HOST TARGET

binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145622 BINDING SITE1 through LOC145622 BINDING SITE3, designated SEQ ID:37907, SEQ ID:37908 and SEQ ID:37915 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67971] Another function of VGAM1959 is therefore inhibition of LOC145622 (Accession XM\_085186). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145622. LOC145732 (Accession XM\_085218) is another VGAM1959 host target gene. LOC145732 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145732, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145732 BINDING SITE, designated SEQ ID:37958, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67972] Another function of VGAM1959 is therefore inhibition of LOC145732 (Accession XM\_085218). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145732. LOC145761 (Accession XM\_096855) is another VGAM1959 host target gene. LOC145761 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145761 BINDING SITE, designated SEQ ID:40583, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67973] Another function of VGAM1959 is therefore inhibition of LOC145761 (Accession XM\_096855). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145761. LOC145815 (Accession XM\_096874) is another VGAM1959 host target gene. LOC145815 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145815, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145815 BINDING SITE, designated SEQ ID:40604, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67974] Another function of VGAM1959 is therefore inhibition of LOC145815 (Accession XM\_096874). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145815. LOC146237 (Accession XM\_096954) is another VGAM1959 host target gene. LOC146237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146237 BINDING SITE, designated SEQ ID:40667, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67975] Another function of VGAM1959 is therefore inhibition of LOC146237 (Accession XM\_096954). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146237. LOC146332 (Accession XM\_085413) is another VGAM1959 host target gene. LOC146332 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146332 BINDING SITE, designated SEQ ID:38130, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67976] Another function of VGAM1959 is therefore inhibition of LOC146332 (Accession XM\_085413). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146332. LOC146452 (Accession XM\_085473) is another VGAM1959 host target gene. LOC146452 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC146452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146452 BINDING SITE, designated SEQ ID:38164, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67977] Another function of VGAM1959 is therefore inhibition of



LOC146452 (Accession XM\_085473). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146452. LOC146488 (Accession XM\_047748) is another VGAM1959 host target gene. LOC146488 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146488, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146488 BINDING SITE, designated SEQ ID:35050, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67978] Another function of VGAM1959 is therefore inhibition of LOC146488 (Accession XM\_047748). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146488. LOC146513 (Accession XM\_097013) is another VGAM1959 host target gene. LOC146513 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC146513 BINDING SITE, designated SEQ ID:40709, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67979] Another function of VGAM1959 is therefore inhibition of LOC146513 (Accession XM\_097013). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146513. LOC146714 (Accession XM\_097072) is another VGAM1959 host target gene. LOC146714 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146714 BINDING SITE, designated SEQ ID:40720, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67980] Another function of VGAM1959 is therefore inhibition of LOC146714 (Accession XM\_097072). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146714. LOC146894 (Accession NM\_145273) is an-

other VGAM1959 host target gene. LOC146894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146894 BINDING SITE, designated SEQ ID:29780, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67981] Another function of VGAM1959 is therefore inhibition of LOC146894 (Accession NM\_145273). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146894. LOC146957 (Accession XM\_085652) is another VGAM1959 host target gene. LOC146957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146957 BINDING SITE, designated SEQ ID:38277, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67982] Another function of VGAM1959 is therefore inhibition of LOC146957 (Accession XM\_085652). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146957. LOC147054 (Accession XM\_097172) is another VGAM1959 host target gene. LOC147054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147054 BINDING SITE, designated SEQ ID:40789, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67983] Another function of VGAM1959 is therefore inhibition of LOC147054 (Accession XM\_097172). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147054. LOC147136 (Accession XM\_085716) is another VGAM1959 host target gene. LOC147136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147136, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147136 BINDING SITE, designated SEQ ID:38303, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67984] Another function of VGAM1959 is therefore inhibition of LOC147136 (Accession XM\_085716). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147136. LOC147165 (Accession XM\_097205) is another VGAM1959 host target gene. LOC147165 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147165, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147165 BINDING SITE, designated SEQ ID:40815, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67985] Another function of VGAM1959 is therefore inhibition of LOC147165 (Accession XM\_097205). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC147165. LOC147178 (Accession XM\_028755) is another VGAM1959 host target gene. LOC147178 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147178 BINDING SITE, designated SEQ ID:30743, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67986] Another function of VGAM1959 is therefore inhibition of LOC147178 (Accession XM\_028755). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147178. LOC147694 (Accession XM\_085843) is another VGAM1959 host target gene. LOC147694 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147694 BINDING SITE, designated SEQ ID:38371, to the nucleotide sequence of VGAM1959 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4670.

[67987] Another function of VGAM1959 is therefore inhibition of LOC147694 (Accession XM\_085843). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147694. LOC147859 (Accession XM\_103235) is another VGAM1959 host target gene. LOC147859 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147859, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147859 BINDING SITE, designated SEQ ID:42151, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67988] Another function of VGAM1959 is therefore inhibition of LOC147859 (Accession XM\_103235). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147859. LOC147993 (Accession XM\_103268) is another VGAM1959 host target gene. LOC147993 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147993, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147993 BINDING SITE, designated SEQ ID:42153, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67989] Another function of VGAM1959 is therefore inhibition of LOC147993 (Accession XM\_103268). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147993. LOC148089 (Accession XM\_086040) is another VGAM1959 host target gene. LOC148089 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148089, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148089 BINDING SITE, designated SEQ ID:38450, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67990] Another function of VGAM1959 is therefore inhibition of LOC148089 (Accession XM\_086040). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC148089. LOC148397 (Accession XM\_086171) is another VGAM1959 host target gene. LOC148397 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC148397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148397 BINDING SITE, designated SEQ ID:38528, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67991] Another function of VGAM1959 is therefore inhibition of LOC148397 (Accession XM\_086171). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148397. LOC148710 (Accession XM\_097506) is another VGAM1959 host target gene. LOC148710 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC148710, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148710 BINDING SITE, designated SEQ ID:40894, to

the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67992] Another function of VGAM1959 is therefore inhibition of LOC148710 (Accession XM\_097506). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148710. LOC148918 (Accession XM\_086361) is another VGAM1959 host target gene. LOC148918 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148918 BINDING SITE, designated SEQ ID:38614, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67993] Another function of VGAM1959 is therefore inhibition of LOC148918 (Accession XM\_086361). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148918. LOC148936 (Accession XM\_097556) is another VGAM1959 host target gene. LOC148936 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC148936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148936 BINDING SITE, designated SEQ ID:40932, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67994] Another function of VGAM1959 is therefore inhibition of LOC148936 (Accession XM\_097556). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148936. LOC148938 (Accession XM\_097555) is another VGAM1959 host target gene. LOC148938 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148938, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148938 BINDING SITE, designated SEQ ID:40925, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67995] Another function of VGAM1959 is therefore inhibition of LOC148938 (Accession XM\_097555). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148938. LOC148979 (Accession XM\_097568) is another VGAM1959 host target gene. LOC148979 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC148979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148979 BINDING SITE, designated SEQ ID:40942, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67996] Another function of VGAM1959 is therefore inhibition of LOC148979 (Accession XM\_097568). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148979. LOC149132 (Accession XM\_086428) is another VGAM1959 host target gene. LOC149132 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC149132 BINDING SITE, designated SEQ ID:38645, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67997] Another function of VGAM1959 is therefore inhibition of LOC149132 (Accession XM\_086428). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149132. LOC149171 (Accession XM\_086450) is another VGAM1959 host target gene. LOC149171 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149171 BINDING SITE, designated SEQ ID:38666, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67998] Another function of VGAM1959 is therefore inhibition of LOC149171 (Accession XM\_086450). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149171. LOC149194 (Accession XM\_086458) is another VGAM1959 host target gene. LOC149194 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149194, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149194 BINDING SITE, designated SEQ ID:38669, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[67999] Another function of VGAM1959 is therefore inhibition of LOC149194 (Accession XM\_086458). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149194. LOC149267 (Accession NM\_138480) is another VGAM1959 host target gene. LOC149267 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149267 BINDING SITE, designated SEQ ID:28831, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68000] Another function of VGAM1959 is therefore inhibition of

LOC149267 (Accession NM\_138480). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149267. LOC149276 (Accession XM\_097621) is another VGAM1959 host target gene. LOC149276 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149276 BINDING SITE, designated SEQ ID:40978, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68001] Another function of VGAM1959 is therefore inhibition of LOC149276 (Accession XM\_097621). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149276. LOC149506 (Accession XM\_097661) is another VGAM1959 host target gene. LOC149506 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC149506 BINDING SITE, designated SEQ ID:41008, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68002] Another function of VGAM1959 is therefore inhibition of LOC149506 (Accession XM\_097661). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149506. LOC149603 (Accession XM\_047499) is another VGAM1959 host target gene. LOC149603 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149603, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149603 BINDING SITE, designated SEQ ID:34971, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68003] Another function of VGAM1959 is therefore inhibition of LOC149603 (Accession XM\_047499). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149603. LOC149620 (Accession XM\_086604) is an-



other VGAM1959 host target gene. LOC149620 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149620 BINDING SITE, designated SEQ ID:38788, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68004] Another function of VGAM1959 is therefore inhibition of LOC149620 (Accession XM\_086604). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149620. LOC149650 (Accession XM\_086623) is another VGAM1959 host target gene. LOC149650 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149650 BINDING SITE, designated SEQ ID:38793, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68005] Another function of VGAM1959 is therefore inhibition of LOC149650 (Accession XM\_086623). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149650. LOC149657 (Accession XM\_097702) is another VGAM1959 host target gene. LOC149657 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149657, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149657 BINDING SITE, designated SEQ ID:41037, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68006] Another function of VGAM1959 is therefore inhibition of LOC149657 (Accession XM\_097702). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149657. LOC150142 (Accession XM\_086791) is another VGAM1959 host target gene. LOC150142 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150142, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150142 BINDING SITE, designated SEQ ID:38851, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68007] Another function of VGAM1959 is therefore inhibition of LOC150142 (Accession XM\_086791). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150142. LOC150150 (Accession XM\_097820) is another VGAM1959 host target gene. LOC150150 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150150, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150150 BINDING SITE, designated SEQ ID:41136, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68008] Another function of VGAM1959 is therefore inhibition of LOC150150 (Accession XM\_097820). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC150150. LOC150372 (Accession XM\_086893) is another VGAM1959 host target gene. LOC150372 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150372, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150372 BINDING SITE, designated SEQ ID:38938, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68009] Another function of VGAM1959 is therefore inhibition of LOC150372 (Accession XM\_086893). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150372. LOC150421 (Accession XM\_097901) is another VGAM1959 host target gene. LOC150421 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150421, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150421 BINDING SITE, designated SEQ ID:41204, to the nucleotide sequence of VGAM1959 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4670.

[68010] Another function of VGAM1959 is therefore inhibition of LOC150421 (Accession XM\_097901). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150421. LOC150776 (Accession XM\_032542) is another VGAM1959 host target gene. LOC150776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150776 BINDING SITE, designated SEQ ID:31677, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68011] Another function of VGAM1959 is therefore inhibition of LOC150776 (Accession XM\_032542). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150776. LOC150819 (Accession XM\_097954) is another VGAM1959 host target gene. LOC150819 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150819, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150819 BINDING SITE, designated SEQ ID:41249, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68012] Another function of VGAM1959 is therefore inhibition of LOC150819 (Accession XM\_097954). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150819. LOC150935 (Accession XM\_087049) is another VGAM1959 host target gene. LOC150935 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150935 BINDING SITE, designated SEQ ID:39021, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68013] Another function of VGAM1959 is therefore inhibition of LOC150935 (Accession XM\_087049). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC150935. LOC151201 (Accession XM\_098021) is another VGAM1959 host target gene. LOC151201 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151201 BINDING SITE, designated SEQ ID:41327, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68014] Another function of VGAM1959 is therefore inhibition of LOC151201 (Accession XM\_098021). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151201. LOC151507 (Accession XM\_087225) is another VGAM1959 host target gene. LOC151507 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151507, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151507 BINDING SITE, designated SEQ ID:39127, to

the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68015] Another function of VGAM1959 is therefore inhibition of LOC151507 (Accession XM\_087225). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151507. LOC151877 (Accession XM\_098132) is another VGAM1959 host target gene. LOC151877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151877 BINDING SITE, designated SEQ ID:41397, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68016] Another function of VGAM1959 is therefore inhibition of LOC151877 (Accession XM\_098132). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151877. LOC152078 (Accession XM\_087376) is another VGAM1959 host target gene. LOC152078 BINDING SITE is HOST TARGET binding site found in the 3' un-



translated region of mRNA encoded by LOC152078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152078 BINDING SITE, designated SEQ ID:39211, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68017] Another function of VGAM1959 is therefore inhibition of LOC152078 (Accession XM\_087376). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152078. LOC152441 (Accession XM\_098230) is another VGAM1959 host target gene. LOC152441 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152441 BINDING SITE, designated SEQ ID:41505, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68018] Another function of VGAM1959 is therefore inhibition of LOC152441 (Accession XM\_098230). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152441. LOC152765 (Accession XM\_087519) is another VGAM1959 host target gene. LOC152765 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152765, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152765 BINDING SITE, designated SEQ ID:39315, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68019] Another function of VGAM1959 is therefore inhibition of LOC152765 (Accession XM\_087519). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152765. LOC153020 (Accession XM\_087578) is another VGAM1959 host target gene. LOC153020 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC153020 BINDING SITE, designated SEQ ID:39354, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68020] Another function of VGAM1959 is therefore inhibition of LOC153020 (Accession XM\_087578). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153020. LOC153339 (Accession XM\_098362) is another VGAM1959 host target gene. LOC153339 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153339, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153339 BINDING SITE, designated SEQ ID:41615, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68021] Another function of VGAM1959 is therefore inhibition of LOC153339 (Accession XM\_098362). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153339. LOC153442 (Accession XM\_098373) is another VGAM1959 host target gene. LOC153442 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153442 BINDING SITE, designated SEQ ID:41636, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68022] Another function of VGAM1959 is therefore inhibition of LOC153442 (Accession XM\_098373). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153442. LOC153577 (Accession XM\_098394) is another VGAM1959 host target gene. LOC153577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153577 BINDING SITE, designated SEQ ID:41643, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68023] Another function of VGAM1959 is therefore inhibition of

LOC153577 (Accession XM\_098394). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153577. LOC153688 (Accession XM\_098416) is another VGAM1959 host target gene. LOC153688 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153688 BINDING SITE, designated SEQ ID:41661, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68024] Another function of VGAM1959 is therefore inhibition of LOC153688 (Accession XM\_098416). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153688. LOC153811 (Accession XM\_087779) is another VGAM1959 host target gene. LOC153811 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC153811 BINDING SITE, designated SEQ ID:39415, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68025] Another function of VGAM1959 is therefore inhibition of LOC153811 (Accession XM\_087779). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153811. LOC154442 (Accession XM\_098536) is another VGAM1959 host target gene. LOC154442 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154442 BINDING SITE, designated SEQ ID:41705, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68026] Another function of VGAM1959 is therefore inhibition of LOC154442 (Accession XM\_098536). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154442. LOC157556 (Accession XM\_098783) is an-

other VGAM1959 host target gene. LOC157556 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157556 BINDING SITE, designated SEQ ID:41821, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68027] Another function of VGAM1959 is therefore inhibition of LOC157556 (Accession XM\_098783). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157556. LOC157623 (Accession XM\_088346) is another VGAM1959 host target gene. LOC157623 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157623, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157623 BINDING SITE, designated SEQ ID:39615, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68028] Another function of VGAM1959 is therefore inhibition of LOC157623 (Accession XM\_088346). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157623. LOC157638 (Accession XM\_088350) is another VGAM1959 host target gene. LOC157638 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157638, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157638 BINDING SITE, designated SEQ ID:39623, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68029] Another function of VGAM1959 is therefore inhibition of LOC157638 (Accession XM\_088350). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157638. LOC157657 (Accession XM\_088352) is another VGAM1959 host target gene. LOC157657 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157657, corresponding to a HOST TARGET binding site such as BIND-



ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157657 BINDING SITE, designated SEQ ID:39626, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68030] Another function of VGAM1959 is therefore inhibition of LOC157657 (Accession XM\_088352). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157657. LOC157773 (Accession XM\_088387) is another VGAM1959 host target gene. LOC157773 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157773 BINDING SITE, designated SEQ ID:39670, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68031] Another function of VGAM1959 is therefore inhibition of LOC157773 (Accession XM\_088387). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC157773. LOC157848 (Accession XM\_088405) is another VGAM1959 host target gene. LOC157848 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157848 BINDING SITE, designated SEQ ID:39672, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68032] Another function of VGAM1959 is therefore inhibition of LOC157848 (Accession XM\_088405). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157848. LOC157860 (Accession XM\_098832) is another VGAM1959 host target gene. LOC157860 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157860 BINDING SITE, designated SEQ ID:41861, to the nucleotide sequence of VGAM1959 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4670.

[68033] Another function of VGAM1959 is therefore inhibition of LOC157860 (Accession XM\_098832). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157860. LOC158056 (Accession XM\_088463) is another VGAM1959 host target gene. LOC158056 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158056 BINDING SITE, designated SEQ ID:39720, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68034] Another function of VGAM1959 is therefore inhibition of LOC158056 (Accession XM\_088463). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158056. LOC158156 (Accession XM\_088496) is another VGAM1959 host target gene. LOC158156 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158156, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158156 BINDING SITE, designated SEQ ID:39739, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68035] Another function of VGAM1959 is therefore inhibition of LOC158156 (Accession XM\_088496). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158156. LOC158332 (Accession XM\_088554) is another VGAM1959 host target gene. LOC158332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158332 BINDING SITE, designated SEQ ID:39825, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68036] Another function of VGAM1959 is therefore inhibition of LOC158332 (Accession XM\_088554). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC158332. LOC158476 (Accession XM\_098955) is another VGAM1959 host target gene. LOC158476 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158476 BINDING SITE, designated SEQ ID:41999, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68037] Another function of VGAM1959 is therefore inhibition of LOC158476 (Accession XM\_098955). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158476. LOC158549 (Accession XM\_098963) is another VGAM1959 host target gene. LOC158549 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC158549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158549 BINDING SITE, designated SEQ ID:42012, to

the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68038] Another function of VGAM1959 is therefore inhibition of LOC158549 (Accession XM\_098963). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158549. LOC160336 (Accession XM\_090228) is another VGAM1959 host target gene. LOC160336 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC160336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160336 BINDING SITE, designated SEQ ID:39996, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68039] Another function of VGAM1959 is therefore inhibition of LOC160336 (Accession XM\_090228). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160336. LOC160414 (Accession XM\_100898) is another VGAM1959 host target gene. LOC160414 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC160414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160414 BINDING SITE, designated SEQ ID:42103, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68040] Another function of VGAM1959 is therefore inhibition of LOC160414 (Accession XM\_100898). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160414. LOC160484 (Accession XM\_090326) is another VGAM1959 host target gene. LOC160484 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC160484, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160484 BINDING SITE, designated SEQ ID:39998, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68041] Another function of VGAM1959 is therefore inhibition of LOC160484 (Accession XM\_090326). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160484. LOC160717 (Accession XM\_090457) is another VGAM1959 host target gene. LOC160717 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC160717, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160717 BINDING SITE, designated SEQ ID:40006, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68042] Another function of VGAM1959 is therefore inhibition of LOC160717 (Accession XM\_090457). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160717. LOC162333 (Accession XM\_102591) is another VGAM1959 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences



of LOC162333 BINDING SITE, designated SEQ ID:42135, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68043] Another function of VGAM1959 is therefore inhibition of LOC162333 (Accession XM\_102591). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC163682 (Accession XM\_099402) is another VGAM1959 host target gene. LOC163682 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC163682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163682 BINDING SITE, designated SEQ ID:42090, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68044] Another function of VGAM1959 is therefore inhibition of LOC163682 (Accession XM\_099402). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163682. LOC165908 (Accession XM\_093523) is another VGAM1959 host target gene. LOC165908 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC165908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165908 BINDING SITE, designated SEQ ID:40196, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68045] Another function of VGAM1959 is therefore inhibition of LOC165908 (Accession XM\_093523). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165908. LOC166793 (Accession NM\_145291) is another VGAM1959 host target gene. LOC166793 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC166793, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166793 BINDING SITE, designated SEQ ID:29806, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68046] Another function of VGAM1959 is therefore inhibition of

LOC166793 (Accession NM\_145291). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166793. LOC166983 (Accession XM\_106422) is another VGAM1959 host target gene. LOC166983 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC166983, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166983 BINDING SITE, designated SEQ ID:42198, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68047] Another function of VGAM1959 is therefore inhibition of LOC166983 (Accession XM\_106422). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166983. LOC170082 (Accession XM\_093092) is another VGAM1959 host target gene. LOC170082 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC170082 BINDING SITE, designated SEQ ID:40173, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68048] Another function of VGAM1959 is therefore inhibition of LOC170082 (Accession XM\_093092). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170082. LOC170221 (Accession XM\_093188) is another VGAM1959 host target gene. LOC170221 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170221 BINDING SITE, designated SEQ ID:40182, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68049] Another function of VGAM1959 is therefore inhibition of LOC170221 (Accession XM\_093188). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170221. LOC170394 (Accession XM\_096329) is an-

other VGAM1959 host target gene. LOC170394 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC170394, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170394 BINDING SITE, designated SEQ ID:40313, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68050] Another function of VGAM1959 is therefore inhibition of LOC170394 (Accession XM\_096329). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170394. LOC195977 (Accession XM\_113625) is another VGAM1959 host target gene. LOC195977 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC195977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC195977 BINDING SITE, designated SEQ ID:42302, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68051] Another function of VGAM1959 is therefore inhibition of LOC195977 (Accession XM\_113625). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC195977. LOC196337 (Accession XM\_113696) is another VGAM1959 host target gene. LOC196337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196337 BINDING SITE, designated SEQ ID:42361, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68052] Another function of VGAM1959 is therefore inhibition of LOC196337 (Accession XM\_113696). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196337. LOC196478 (Accession XM\_113729) is another VGAM1959 host target gene. LOC196478 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196478, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196478 BINDING SITE, designated SEQ ID:42378, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68053] Another function of VGAM1959 is therefore inhibition of LOC196478 (Accession XM\_113729). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196478. LOC196510 (Accession XM\_113738) is another VGAM1959 host target gene. LOC196510 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196510, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196510 BINDING SITE, designated SEQ ID:42394, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68054] Another function of VGAM1959 is therefore inhibition of LOC196510 (Accession XM\_113738). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196510. LOC196812 (Accession XM\_116868) is another VGAM1959 host target gene. LOC196812 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196812 BINDING SITE, designated SEQ ID:43133, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68055] Another function of VGAM1959 is therefore inhibition of LOC196812 (Accession XM\_116868). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196812. LOC196860 (Accession XM\_116945) is another VGAM1959 host target gene. LOC196860 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196860 BINDING SITE, designated SEQ ID:43153, to the nucleotide sequence of VGAM1959 RNA, herein desig-



nated VGAM RNA, also designated SEQ ID:4670.

[68056] Another function of VGAM1959 is therefore inhibition of LOC196860 (Accession XM\_116945). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196860. LOC196872 (Accession XM\_113760) is another VGAM1959 host target gene. LOC196872 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196872 BINDING SITE, designated SEQ ID:42419, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68057] Another function of VGAM1959 is therefore inhibition of LOC196872 (Accession XM\_113760). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196872. LOC196957 (Accession XM\_113789) is another VGAM1959 host target gene. LOC196957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196957, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196957 BINDING SITE, designated SEQ ID:42430, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68058] Another function of VGAM1959 is therefore inhibition of LOC196957 (Accession XM\_113789). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196957. LOC196961 (Accession XM\_113790) is another VGAM1959 host target gene. LOC196961 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196961 BINDING SITE, designated SEQ ID:42439, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68059] Another function of VGAM1959 is therefore inhibition of LOC196961 (Accession XM\_113790). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC196961. LOC197138 (Accession XM\_113829) is another VGAM1959 host target gene. LOC197138 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC197138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197138 BINDING SITE, designated SEQ ID:42457, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68060] Another function of VGAM1959 is therefore inhibition of LOC197138 (Accession XM\_113829). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197138. LOC197273 (Accession XM\_041139) is another VGAM1959 host target gene. LOC197273 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC197273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197273 BINDING SITE, designated SEQ ID:33472, to

the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68061] Another function of VGAM1959 is therefore inhibition of LOC197273 (Accession XM\_041139). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197273. LOC197342 (Accession XM\_113869) is another VGAM1959 host target gene. LOC197342 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197342 BINDING SITE, designated SEQ ID:42485, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68062] Another function of VGAM1959 is therefore inhibition of LOC197342 (Accession XM\_113869). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197342. LOC199704 (Accession XM\_113994) is another VGAM1959 host target gene. LOC199704 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC199704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199704 BINDING SITE, designated SEQ ID:42605, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68063] Another function of VGAM1959 is therefore inhibition of LOC199704 (Accession XM\_113994). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199704. LOC199733 (Accession XM\_117123) is another VGAM1959 host target gene. LOC199733 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199733, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199733 BINDING SITE, designated SEQ ID:43245, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68064] Another function of VGAM1959 is therefore inhibition of LOC199733 (Accession XM\_117123). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199733. LOC199858 (Accession XM\_114040) is another VGAM1959 host target gene. LOC199858 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199858 BINDING SITE, designated SEQ ID:42635, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68065] Another function of VGAM1959 is therefore inhibition of LOC199858 (Accession XM\_114040). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199858. LOC199920 (Accession XM\_114056) is another VGAM1959 host target gene. LOC199920 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC199920 BINDING SITE, designated SEQ ID:42662, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68066] Another function of VGAM1959 is therefore inhibition of LOC199920 (Accession XM\_114056). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199920. LOC199990 (Accession XM\_114083) is another VGAM1959 host target gene. LOC199990 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199990, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199990 BINDING SITE, designated SEQ ID:42680, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68067] Another function of VGAM1959 is therefore inhibition of LOC199990 (Accession XM\_114083). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199990. LOC200059 (Accession XM\_114104) is another VGAM1959 host target gene. LOC200059 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200059, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200059 BINDING SITE, designated SEQ ID:42702, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68068] Another function of VGAM1959 is therefore inhibition of LOC200059 (Accession XM\_114104). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200059. LOC200093 (Accession XM\_032184) is another VGAM1959 host target gene. LOC200093 BINDING SITE1 and LOC200093 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC200093, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200093 BINDING SITE1 and LOC200093 BINDING SITE2, designated SEQ ID:31599 and SEQ ID:31605 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA,



also designated SEQ ID:4670.

[68069] Another function of VGAM1959 is therefore inhibition of LOC200093 (Accession XM\_032184). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200093. LOC200220 (Accession XM\_114157) is another VGAM1959 host target gene. LOC200220 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200220 BINDING SITE, designated SEQ ID:42743, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68070] Another function of VGAM1959 is therefore inhibition of LOC200220 (Accession XM\_114157). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200220. LOC200953 (Accession XM\_117302) is another VGAM1959 host target gene. LOC200953 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200953, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200953 BINDING SITE, designated SEQ ID:43366, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68071] Another function of VGAM1959 is therefore inhibition of LOC200953 (Accession XM\_117302). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200953. LOC201382 (Accession XM\_113963) is another VGAM1959 host target gene. LOC201382 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201382 BINDING SITE, designated SEQ ID:42573, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68072] Another function of VGAM1959 is therefore inhibition of LOC201382 (Accession XM\_113963). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC201382. LOC201627 (Accession XM\_114353) is another VGAM1959 host target gene. LOC201627 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201627 BINDING SITE, designated SEQ ID:42897, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68073] Another function of VGAM1959 is therefore inhibition of LOC201627 (Accession XM\_114353). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201627. LOC201911 (Accession XM\_117339) is another VGAM1959 host target gene. LOC201911 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201911, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201911 BINDING SITE, designated SEQ ID:43392, to

the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68074] Another function of VGAM1959 is therefore inhibition of LOC201911 (Accession XM\_117339). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201911. LOC204804 (Accession XM\_115599) is another VGAM1959 host target gene. LOC204804 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204804, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204804 BINDING SITE, designated SEQ ID:43099, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68075] Another function of VGAM1959 is therefore inhibition of LOC204804 (Accession XM\_115599). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204804. LOC204820 (Accession XM\_119323) is another VGAM1959 host target gene. LOC204820 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC204820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204820 BINDING SITE, designated SEQ ID:43584, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68076] Another function of VGAM1959 is therefore inhibition of LOC204820 (Accession XM\_119323). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204820. LOC206463 (Accession XM\_116523) is another VGAM1959 host target gene. LOC206463 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC206463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC206463 BINDING SITE, designated SEQ ID:43123, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68077] Another function of VGAM1959 is therefore inhibition of LOC206463 (Accession XM\_116523). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC206463. LOC219793 (Accession XM\_166127) is another VGAM1959 host target gene. LOC219793 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC219793, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219793 BINDING SITE, designated SEQ ID:43916, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68078] Another function of VGAM1959 is therefore inhibition of LOC219793 (Accession XM\_166127). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219793. LOC220018 (Accession XM\_167816) is another VGAM1959 host target gene. LOC220018 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC220018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC220018 BINDING SITE, designated SEQ ID:44854, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68079] Another function of VGAM1959 is therefore inhibition of LOC220018 (Accession XM\_167816). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220018. LOC220020 (Accession XM\_167821) is another VGAM1959 host target gene. LOC220020 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220020 BINDING SITE, designated SEQ ID:44864, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68080] Another function of VGAM1959 is therefore inhibition of LOC220020 (Accession XM\_167821). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220020. LOC220705 (Accession XM\_166000) is another VGAM1959 host target gene. LOC220705 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220705 BINDING SITE, designated SEQ ID:43833, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68081] Another function of VGAM1959 is therefore inhibition of LOC220705 (Accession XM\_166000). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220705. LOC220766 (Accession XM\_165471) is another VGAM1959 host target gene. LOC220766 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220766 BINDING SITE, designated SEQ ID:43657, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68082] Another function of VGAM1959 is therefore inhibition of



LOC220766 (Accession XM\_165471). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220766. LOC221143 (Accession XM\_167986) is another VGAM1959 host target gene. LOC221143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221143 BINDING SITE, designated SEQ ID:44943, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68083] Another function of VGAM1959 is therefore inhibition of LOC221143 (Accession XM\_167986). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221143. LOC221178 (Accession XM\_167936) is another VGAM1959 host target gene. LOC221178 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC221178 BINDING SITE, designated SEQ ID:44928, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68084] Another function of VGAM1959 is therefore inhibition of LOC221178 (Accession XM\_167936). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221178. LOC221415 (Accession XM\_168137) is another VGAM1959 host target gene. LOC221415 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221415 BINDING SITE, designated SEQ ID:45064, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68085] Another function of VGAM1959 is therefore inhibition of LOC221415 (Accession XM\_168137). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221415. LOC221496 (Accession XM\_166338) is an-

other VGAM1959 host target gene. LOC221496 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221496, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221496 BINDING SITE, designated SEQ ID:44177, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68086] Another function of VGAM1959 is therefore inhibition of LOC221496 (Accession XM\_166338). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221496. LOC221692 (Accession XM\_166420) is another VGAM1959 host target gene. LOC221692 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221692, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221692 BINDING SITE, designated SEQ ID:44297, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68087] Another function of VGAM1959 is therefore inhibition of LOC221692 (Accession XM\_166420). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221692. LOC221756 (Accession XM\_166394) is another VGAM1959 host target gene. LOC221756 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221756, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221756 BINDING SITE, designated SEQ ID:44241, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68088] Another function of VGAM1959 is therefore inhibition of LOC221756 (Accession XM\_166394). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221756. LOC221922 (Accession XM\_166555) is another VGAM1959 host target gene. LOC221922 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221922, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221922 BINDING SITE, designated SEQ ID:44533, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68089] Another function of VGAM1959 is therefore inhibition of LOC221922 (Accession XM\_166555). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221922. LOC222060 (Accession XM\_168427) is another VGAM1959 host target gene. LOC222060 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222060 BINDING SITE, designated SEQ ID:45162, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68090] Another function of VGAM1959 is therefore inhibition of LOC222060 (Accession XM\_168427). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC222060. LOC222134 (Accession XM\_168432) is another VGAM1959 host target gene. LOC222134 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222134 BINDING SITE, designated SEQ ID:45171, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68091] Another function of VGAM1959 is therefore inhibition of LOC222134 (Accession XM\_168432). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222134. LOC222602 (Accession XM\_167171) is another VGAM1959 host target gene. LOC222602 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222602, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222602 BINDING SITE, designated SEQ ID:44618, to the nucleotide sequence of VGAM1959 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4670.

[68092] Another function of VGAM1959 is therefore inhibition of LOC222602 (Accession XM\_167171). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222602. LOC245727 (Accession XM\_165913) is another VGAM1959 host target gene. LOC245727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC245727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245727 BINDING SITE, designated SEQ ID:43798, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68093] Another function of VGAM1959 is therefore inhibition of LOC245727 (Accession XM\_165913). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245727. LOC245728 (Accession XM\_165922) is another VGAM1959 host target gene. LOC245728 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC245728, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245728 BINDING SITE, designated SEQ ID:43802, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68094] Another function of VGAM1959 is therefore inhibition of LOC245728 (Accession XM\_165922). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245728. LOC245771 (Accession XM\_167366) is another VGAM1959 host target gene. LOC245771 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC245771, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245771 BINDING SITE, designated SEQ ID:44636, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68095] Another function of VGAM1959 is therefore inhibition of LOC245771 (Accession XM\_167366). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treat-



ment of diseases and clinical conditions associated with LOC245771. LOC253001 (Accession XM\_171711) is another VGAM1959 host target gene. LOC253001 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC253001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253001 BINDING SITE, designated SEQ ID:46060, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68096] Another function of VGAM1959 is therefore inhibition of LOC253001 (Accession XM\_171711). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253001. LOC253216 (Accession XM\_170765) is another VGAM1959 host target gene. LOC253216 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC253216, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253216 BINDING SITE, designated SEQ ID:45521, to

the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68097] Another function of VGAM1959 is therefore inhibition of LOC253216 (Accession XM\_170765). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253216. LOC253539 (Accession XM\_171134) is another VGAM1959 host target gene. LOC253539 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253539, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253539 BINDING SITE, designated SEQ ID:45939, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68098] Another function of VGAM1959 is therefore inhibition of LOC253539 (Accession XM\_171134). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253539. LOC254228 (Accession XM\_171123) is another VGAM1959 host target gene. LOC254228 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC254228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254228 BINDING SITE, designated SEQ ID:45921, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68099] Another function of VGAM1959 is therefore inhibition of LOC254228 (Accession XM\_171123). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254228. LOC255452 (Accession XM\_174088) is another VGAM1959 host target gene. LOC255452 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255452 BINDING SITE, designated SEQ ID:46574, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68100] Another function of VGAM1959 is therefore inhibition of LOC255452 (Accession XM\_174088). Accordingly, utilities

of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255452. LOC255458 (Accession XM\_173150) is another VGAM1959 host target gene. LOC255458 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255458, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255458 BINDING SITE, designated SEQ ID:46407, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68101] Another function of VGAM1959 is therefore inhibition of LOC255458 (Accession XM\_173150). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255458. LOC255535 (Accession XM\_171034) is another VGAM1959 host target gene. LOC255535 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC255535 BINDING SITE, designated SEQ ID:45807, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68102] Another function of VGAM1959 is therefore inhibition of LOC255535 (Accession XM\_171034). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255535. LOC255743 (Accession XM\_171089) is another VGAM1959 host target gene. LOC255743 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255743 BINDING SITE, designated SEQ ID:45902, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68103] Another function of VGAM1959 is therefore inhibition of LOC255743 (Accession XM\_171089). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255743. LOC256158 (Accession XM\_175125) is another VGAM1959 host target gene. LOC256158 BINDING

SITE1 through LOC256158 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC256158, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE1 through LOC256158 BINDING SITE3, designated SEQ ID:46622, SEQ ID:46623 and SEQ ID:46632 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68104] Another function of VGAM1959 is therefore inhibition of LOC256158 (Accession XM\_175125). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256158. LOC256307 (Accession XM\_173118) is another VGAM1959 host target gene. LOC256307 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256307, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256307 BINDING SITE, designated SEQ ID:46370, to the nucleotide sequence of VGAM1959 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4670.

[68105] Another function of VGAM1959 is therefore inhibition of LOC256307 (Accession XM\_173118). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256307. LOC256492 (Accession XM\_174467) is another VGAM1959 host target gene. LOC256492 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256492, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256492 BINDING SITE, designated SEQ ID:46592, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68106] Another function of VGAM1959 is therefore inhibition of LOC256492 (Accession XM\_174467). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256492. LOC256781 (Accession XM\_174695) is another VGAM1959 host target gene. LOC256781 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256781, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256781 BINDING SITE, designated SEQ ID:46602, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68107] Another function of VGAM1959 is therefore inhibition of LOC256781 (Accession XM\_174695). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256781. LOC256867 (Accession XM\_170694) is another VGAM1959 host target gene. LOC256867 BINDING SITE1 and LOC256867 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC256867, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256867 BINDING SITE1 and LOC256867 BINDING SITE2, designated SEQ ID:45473 and SEQ ID:45476 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68108] Another function of VGAM1959 is therefore inhibition of



LOC256867 (Accession XM\_170694). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256867. LOC51308 (Accession NM\_016606) is another VGAM1959 host target gene. LOC51308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51308 BINDING SITE, designated SEQ ID:18710, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68109] Another function of VGAM1959 is therefore inhibition of LOC51308 (Accession NM\_016606). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51308. LOC51334 (Accession NM\_016644) is another VGAM1959 host target gene. LOC51334 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51334, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC51334 BINDING SITE, designated SEQ ID:18751, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68110] Another function of VGAM1959 is therefore inhibition of LOC51334 (Accession NM\_016644). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51334. LOC85028 (Accession NM\_053040) is another VGAM1959 host target gene. LOC85028 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC85028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC85028 BINDING SITE, designated SEQ ID:27585, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68111] Another function of VGAM1959 is therefore inhibition of LOC85028 (Accession NM\_053040). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC85028. LOC90249 (Accession XM\_030300) is another

VGAM1959 host target gene. LOC90249 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90249 BINDING SITE, designated SEQ ID:31008, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68112] Another function of VGAM1959 is therefore inhibition of LOC90249 (Accession XM\_030300). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90249. LOC90342 (Accession XM\_031009) is another VGAM1959 host target gene. LOC90342 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90342 BINDING SITE, designated SEQ ID:31257, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68113] Another function of VGAM1959 is therefore inhibition of LOC90342 (Accession XM\_031009). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90342. LOC90826 (Accession XM\_034321) is another VGAM1959 host target gene. LOC90826 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90826 BINDING SITE, designated SEQ ID:32050, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68114] Another function of VGAM1959 is therefore inhibition of LOC90826 (Accession XM\_034321). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90826. LOC91040 (Accession XM\_035641) is another VGAM1959 host target gene. LOC91040 BINDING SITE1 and LOC91040 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC91040, corresponding to HOST TARGET binding sites

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91040 BINDING SITE1 and LOC91040 BINDING SITE2, designated SEQ ID:32316 and SEQ ID:32322 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68115] Another function of VGAM1959 is therefore inhibition of LOC91040 (Accession XM\_035641). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91040. LOC91355 (Accession XM\_037825) is another VGAM1959 host target gene. LOC91355 BINDING SITE1 and LOC91355 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC91355, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91355 BINDING SITE1 and LOC91355 BINDING SITE2, designated SEQ ID:32705 and SEQ ID:32808 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68116] Another function of VGAM1959 is therefore inhibition of LOC91355 (Accession XM\_037825). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91355. LOC91464 (Accession XM\_038589) is another VGAM1959 host target gene. LOC91464 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91464 BINDING SITE, designated SEQ ID:32874, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68117] Another function of VGAM1959 is therefore inhibition of LOC91464 (Accession XM\_038589). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91464. LOC91565 (Accession XM\_039231) is another VGAM1959 host target gene. LOC91565 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91565, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91565 BINDING SITE, designated SEQ ID:33023, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68118] Another function of VGAM1959 is therefore inhibition of LOC91565 (Accession XM\_039231). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91565. LOC91782 (Accession XM\_040612) is another VGAM1959 host target gene. LOC91782 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91782 BINDING SITE, designated SEQ ID:33336, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68119] Another function of VGAM1959 is therefore inhibition of LOC91782 (Accession XM\_040612). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC91782. LOC91828 (Accession XM\_040910) is another VGAM1959 host target gene. LOC91828 BINDING SITE1 and LOC91828 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC91828, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91828 BINDING SITE1 and LOC91828 BINDING SITE2, designated SEQ ID:33407 and SEQ ID:33409 respectively, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68120] Another function of VGAM1959 is therefore inhibition of LOC91828 (Accession XM\_040910). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91828. LOC92162 (Accession XM\_043273) is another VGAM1959 host target gene. LOC92162 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC92162, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of



LOC92162 BINDING SITE, designated SEQ ID:33921, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68121] Another function of VGAM1959 is therefore inhibition of LOC92162 (Accession XM\_043273). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92162. LOC92230 (Accession XM\_043733) is another VGAM1959 host target gene. LOC92230 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92230, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92230 BINDING SITE, designated SEQ ID:34007, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68122] Another function of VGAM1959 is therefore inhibition of LOC92230 (Accession XM\_043733). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92230. LOC93109 (Accession XM\_049278) is another VGAM1959 host target gene. LOC93109 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93109, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93109 BINDING SITE, designated SEQ ID:35374, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68123] Another function of VGAM1959 is therefore inhibition of LOC93109 (Accession XM\_049278). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93109. LOC93444 (Accession XM\_051455) is another VGAM1959 host target gene. LOC93444 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93444, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93444 BINDING SITE, designated SEQ ID:35844, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68124] Another function of VGAM1959 is therefore inhibition of

LOC93444 (Accession XM\_051455). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93444. LOC95702 (Accession XM\_031446) is another VGAM1959 host target gene. LOC95702 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC95702, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC95702 BINDING SITE, designated SEQ ID:31384, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68125] Another function of VGAM1959 is therefore inhibition of LOC95702 (Accession XM\_031446). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC95702. LOC96597 (Accession XM\_039922) is another VGAM1959 host target gene. LOC96597 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC96597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC96597 BINDING SITE, designated SEQ ID:33233, to the nucleotide sequence of VGAM1959 RNA, herein designated VGAM RNA, also designated SEQ ID:4670.

[68126] Another function of VGAM1959 is therefore inhibition of LOC96597 (Accession XM\_039922). Accordingly, utilities of VGAM1959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC96597. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1960 (VGAM1960) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[68127] VGAM1960 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1960 was detected is described hereinabove with reference to Figs. 1–8.

[68128] VGAM1960 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1960 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[68129] VGAM1960 gene encodes a VGAM1960 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1960 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1960 precursor RNA is designated SEQ ID:1946, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1946 is located at position 10523 relative to the genome of Macaca Mulatta Rhadinovirus.

[68130] VGAM1960 precursor RNA folds onto itself, forming VGAM1960 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[68131] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1960 folded precursor RNA into VGAM1960 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1960 RNA is designated SEQ ID:4671, and is provided hereinbelow with reference to the sequence listing part.

[68132] VGAM1960 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1960 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1960 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[68133] VGAM1960 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1960 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1960 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1960 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1960 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[68134] The complementary binding of VGAM1960 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1960 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1960 host target RNA into VGAM1960 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[68135] It is appreciated that VGAM1960 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1960 host target genes. The mRNA of each one of this plurality of VGAM1960 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1960 RNA, herein designated VGAM RNA, and which when bound by VGAM1960 RNA causes inhibition of translation of respective one or more VGAM1960 host target proteins.

[68136] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1960 gene, herein designated VGAM GENE, on one or more VGAM1960 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-



though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[68137] It is yet further appreciated that a function of VGAM1960 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1960 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1960 correlate with, and may be deduced from, the identity of the host target genes which VGAM1960 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[68138] Nucleotide sequences of the VGAM1960 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1960 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1960 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1960 are further described hereinbelow with reference to Table 1.

[68139] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1960 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1960 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[68140] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1960 gene, herein designated VGAM is inhibition of expression of VGAM1960 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1960 correlate with, and may be deduced from, the identity of the target genes which VGAM1960 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[68141] Angiotensin II Receptor, Type 1 (AGTR1, Accession NM\_000685) is a VGAM1960 host target gene. AGTR1 BINDING SITE1 through AGTR1 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AGTR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGTR1 BINDING SITE1 through AGTR1 BINDING SITE5, designated SEQ ID:6342, SEQ ID:11243, SEQ ID:14309, SEQ ID:25594 and SEQ

ID:25769 respectively, to the nucleotide sequence of VGAM1960 RNA, herein designated VGAM RNA, also designated SEQ ID:4671.

[68142] A function of VGAM1960 is therefore inhibition of Angiotensin II Receptor, Type 1 (AGTR1, Accession NM\_000685), a gene which is an important effector controlling blood pressure and volume in the cardiovascular system. Accordingly, utilities of VGAM1960 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGTR1. The function of AGTR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM96. Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM\_042963) is another VGAM1960 host target gene. ARHGEF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF6 BINDING SITE, designated SEQ ID:33848, to the nucleotide sequence of VGAM1960 RNA, herein designated VGAM RNA, also designated SEQ

ID:4671.

[68143] Another function of VGAM1960 is therefore inhibition of Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM\_042963). Accordingly, utilities of VGAM1960 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF6. Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession NM\_138271) is another VGAM1960 host target gene. ATRX BINDING SITE1 and ATRX BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ATRX, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATRX BINDING SITE1 and ATRX BINDING SITE2, designated SEQ ID:28685 and SEQ ID:6096 respectively, to the nucleotide sequence of VGAM1960 RNA, herein designated VGAM RNA, also designated SEQ ID:4671.

[68144] Another function of VGAM1960 is therefore inhibition of Alpha Thalassemia/mental Retardation Syndrome X-linked (RAD54 homolog, *S. cerevisiae*) (ATRX, Accession NM\_138271). Accordingly, utilities of VGAM1960 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with ATRX. Caldesmon 1 (CALD1, Accession NM\_033138) is another VGAM1960 host target gene. CALD1 BINDING SITE1 and CALD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CALD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALD1 BINDING SITE1 and CALD1 BINDING SITE2, designated SEQ ID:26992 and SEQ ID:27010 respectively, to the nucleotide sequence of VGAM1960 RNA, herein designated VGAM RNA, also designated SEQ ID:4671.

[68145] Another function of VGAM1960 is therefore inhibition of Caldesmon 1 (CALD1, Accession NM\_033138), a gene which is implicated in the regulation of actomyosin interactions in smooth muscle and nonmuscle cells. Accordingly, utilities of VGAM1960 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALD1. The function of CALD1 has been established by previous studies. Caldesmon is a potential actomyosin regulatory protein found in smooth muscle and nonmuscle cells. Domain mapping and physical studies

suggested that CDM is an elongated molecule with an N-terminal myosin/calmodulin-binding domain and a C-terminal tropomyosin/actin/calmodulin-binding domain separated by a 40-nm-long central helix. Humphrey et al. (1992) used a probe encoding part of avian caldesmon to screen a human aorta library and clone smooth-muscle and nonmuscle CDM-encoding cDNAs. The predicted smooth-muscle polypeptide is 793 amino acids long. As in the case of chicken CDM, nonmuscle CDM was missing the central helical domain of 256 amino acids. The non-muscle form appeared to be generated by exon skipping. Humphrey et al. (1992) suggested that the CDMs are a small family of highly conserved proteins which are probably derived from a single gene. The high molecular weight caldesmon is predominantly expressed in smooth muscles, whereas the low molecular weight caldesmon is widely distributed in nonmuscle tissues and cells. Hayashi et al. (1992) demonstrated that the human CDM gene is composed of 14 exons. By fluorescence in situ hybridization, they showed that it is encoded by a single gene located at 7q33-q34. The regulation of high molecular weight and low molecular weight caldesmon expression was thought to depend on selection of the 2 5-prime

splice sites within exon 3.

[68146] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[68147] Hayashi, K.; Yano, H.; Hashida, T.; Takeuchi, R.; Takeda, O.; Asada, K.; Takahashi, E.; Kato, I.; Sobue, K. : Genomic structure of the human caldesmon gene. Proc. Nat. Acad. Sci. 89: 12122–12126, 1992. ; and

[68148] Humphrey, M. B.; Herrera-Sosa, H.; Gonzalez, G.; Lee, R.; Bryan, J. : Cloning of cDNAs encoding human caldesmons. Gene 112: 197–204, 1992.

[68149] Further studies establishing the function and utilities of CALD1 are found in John Hopkins OMIM database record ID 114213, and in cited publications numbered 4030–4031 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dihydropyrimidinase-like 2 (DPYSL2, Accession NM\_001386) is another VGAM1960 host target gene. DPYSL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DPYSL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide